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Experiments towards the synthesis of corrins. Part II. The preparation and reactions of Δ^1-pyrroline 1-oxides. By R. BONNETT, R. F. C. BROWN, V. M. CLARK, I. O. SUTHERLAND, and SIR ALEXANDER TODD

Experiments towards the synthesis of corrins. Part III. Formation of a bicyclic oxaziran from a Δ^1-pyrroline and from the corresponding nitrone. By R. BONNETT, V. M. CLARK, and SIR ALEXANDER TODD

Experiments towards the synthesis of corrins. Part IV. The oxidation and ring expansion of 2 : 4 : 4-trimethyl-Δ^1-pyrroline 1-oxide. By R. F. C. BROWN, V. M. CLARK, and SIR ALEXANDER TODD

Experiments towards the synthesis of corrins. Part V. The base-catalysed aldol-type reactions of Δ^1-pyrroline 1-oxides. By R. F. C. BROWN, V. M. CLARK, I. O. SUTHERLAND, and SIR ALEXANDER TODD

Experiments towards the synthesis of corrins. Part VI. The dimerisation of Δ^1-pyrroline 1-oxides to 2-(1-hydroxy-2-pyrrolidinyl)-Δ^1-pyrroline 1-oxides. By R. F. C. BROWN, V. M. CLARK, M. LAMCHEN, and SIR ALEXANDER TODD

Experiments towards the synthesis of corrins. Part VII. The reductive dimerisation of a Δ^1-pyrroline 1-oxide. Oxidative degradation of 2 : 2′- and 2 : 3′-bipyrrolidinyl derivatives. By V. M. CLARK, B. SKLARZ, and SIR ALEXANDER TODD

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Acyl isothiocyanates. Part III. Properties of some phosphoroisothiocyanatidates. By D. T. ELMORE and J. R. OGLE

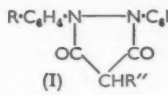
The structure of *pseudo*morphine. By K. W. BENTLEY and S. F. DYKE

261. *Derivatives of 3 : 5-Dioxopyrazolidine likely to possess Therapeutic Activity.*[1]

By W. H. Linnell and M. Khalifa.

pp'-Dinitrohydrazobenzene condensed with *n*-propyl- and *n*-butylmalonyl dichlorides, giving high yields of 3 : 5-dioxopyrazolidine derivatives. Other hydrazo-compounds were similarly cyclised.

Although 4-*n*-butyl-1 : 2-diphenyl-3 : 5-dioxopyrazolidine (phenylbutazone: I; R = R' = H, R'' = Bu^n) is of value in the treatment of rheumatoid arthritis and allied conditions,[2] it has pronounced toxic side effects [3,4] and the need arose for a less toxic substitute. In the hope that introduction of appropriate substituents in the phenyl groups



(I)

(R and R' may be the same or different. R and R' = H, NHAc, OAc, OBz, CO_2H : R'' = Pr^n, Bu^n.)

of phenylbutazone would give a more suitable product, derivatives having the above general formula were synthesised, by cyclising substituted hydrazobenzenes with alkylmalonyl chlorides. The hydrazo-compounds were obtained by reducing the corresponding azo- or azoxy-derivatives. An attempt to prepare *pp'*-dinitroazobenzene by Green and Bearder's method [5] did not give satisfactory results. However, this azo-compound was obtained in 15% yield by oxidising *p*-nitroaniline with aqueous potassium permanganate; [6] but when the permanganate was replaced by ammonium persulphate and the oxidation was carried out in neutral medium *pp'*-dinitroazoxybenzene was afforded in 48% yield.[7] Oxidation in acid solution gave a 92% yield.

The alkylmalonyl chlorides were prepared by alkylation of ethyl malonate,[8] hydrolysis of the resulting esters to the acids,[9] and conversion of these into the corresponding acid chlorides by treatment with thionyl chloride.[10]

Condensation of *pp'*-dinitrohydrazobenzene with diethyl alkylmalonates in the presence of sodium ethoxide resulted in oxidation of the hydrazo-compound, probably owing to its tautomerisation to a readily oxidisable quinonoid form.[5] With alkylmalonyl chlorides in ether–pyridine (Geigy [11]) cyclisation did not occur. However, it was achieved in dry benzene at the reflux temperature. Reduction of the nitro-groups in the pyrazolidine derivative thus obtained (I; R = R' = NO_2, R'' = Pr^n or Bu^n) was accomplished with zinc dust and ammonium chloride.[12] The reduction product was always contaminated with zinc salts, which could be removed after acetylation. An attempt to convert the amino- into hydroxy-groups was unsuccessful. Nevertheless, derivatives of such hydroxy-compounds (I; R = R' = OAc or OBz) were obtained by condensing acyl derivatives of *p*-hydrazophenol with alkylmalonyl chlorides. This condensation was rendered difficult by the ease with which the hydrazo-compound was oxidised and its poor solubility in solvents recommended for such condensations. Use of an atmosphere of nitrogen did not avoid oxidation of the hydrazo-compound, especially when heat was applied. This

[1] Khalifa, Dissertation, London, 1955.
[2] Currie, *Lancet*, 1952, ii, 15.
[3] Kuzell, Schaffarzick, Brown, and Manble, *J. Amer. Med. Assoc.*, 1952, **149**, 729.
[4] Barter, Gee, and Hirson, *Brit. Med. J.*, 1952, ii, 1392.
[5] Green and Bearder, *J.*, 1911, **99**, 1967.
[6] Cf. Laar, *Ber.*, 1881, **14**, 1928.
[7] Bamberger and Hübner, *Ber.*, 1903, **36**, 3808.
[8] *Org. Synth.*, Coll. Vol. I, 2nd Edn., p. 250; Coll. Vol. II, p. 279
[9] Cf. *op. cit.*, Coll. Vol. II, p. 93.
[10] Cf. Staudinger and Bereza, *Ber.*, 1908, **41**, 4463.
[11] Geigy, Swiss P. 267,222 (1950).
[12] Cf. Morgan and Hickinbottom, *J.*, 1921, **119**, 1883.

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difficulty, however, was overcome by addition of a trace of zinc dust to the reaction mixture. Acetic anhydride was the best solvent for the condensation because of the appreciable solubility of the hydrazo-compound in it and of the possibility that it might acetylate the hydrazo-compound, thus rendering it less susceptible to oxidation.

Experimental

(All m. p.s are uncorrected.)

pp'-Dinitroazobenzene.—*p*-Nitroaniline (20 g.) was almost dissolved in boiling water (2 l.) and powdered potassium permanganate (32 g.) was gradually added with brisk stirring. The reaction was continued for 5 hr. at 90—100°. Unreacted *p*-nitroaniline (7 g.) was recovered on concentration of the filtrate. The precipitated manganese dioxide was extracted with acetone, and the extract yielded pure *pp'*-dinitroazobenzene (3 g.), m. p. 216° (lit.,[13] 214—216°).

pp'-Dinitroazoxybenzene.—Finely powdered ammonium persulphate (24 g.) was stirred into ice-cold concentrated sulphuric acid (20 ml.), and when the mixture was homogeneous crushed ice (140 g.) was added, followed by *p*-nitroaniline (4·6 g.) added all at once with brisk stirring. The mixture was kept for 12 hr. at room temperature, then diluted with an equal volume of water. The crude product (4·5 g.) was steam distilled to remove *p*-dinitrobenzene (*ca.* 0·3 g.; m. p. 173—174°) and the residue, after one crystallisation from benzene, had m. p. 190—192° (lit.,[7] 190—192°).

pp'-Dihydroxyazobenzene and its diacetyl and dibenzoyl derivatives were prepared according to recorded methods.[14] Azobenzene-*p*-carboxylic acid was prepared by Anspon's method,[15] which is essentially that described by Angeli and Valori.[16] *pp'*-Dinitrohydrazobenzene was obtained by reducing the corresponding azo- or azoxy-derivative with alcoholic ammonium sulphide according to Werner and Stiasny's method.[17] Crystallisation from acetone gave yellow prisms, m. p. 248—250° (lit.,[19] 248—250°). Diacetyl- and dibenzoyl-*p*-hydrazophenol, prepared by reducing the azo-derivatives with zinc dust and acetic acid according to Khalifa and Linnell's modification [19] of Jacobsen and Steinbrenk's method,[20] melted at 138—140° and 188—190° respectively. Hydrazobenzene-*p*-carboxylic acid, prepared by the above modified procedure, had m. p. 194—195° (lit.,[20] 192—193°).

3 : 5-Dioxopyrazolidine derivative (I)		Method		Yield		Found (%)			Required (%)		
R = R′	R″	of prepn.	M. p.	(%)	Formula	C	H	N	C	H	N
p-NO_2	Pr^n	1	177—178°	85	$C_{18}H_{16}O_6N_4$	56·2	4·5	14·6	56·3	4·2	14·6
,,	Bu^n	1	157—158	85	$C_{19}H_{18}O_6N_4$	57·9	4·5	14·3	57·3	4·5	14·1
p-NHAc	Pr^n		234—236		$C_{22}H_{24}O_4N_4$	64·2	6·0	13·5	64·7	5·9	13·7
,,	Bu^n		216—218		$C_{23}H_{26}O_4N_4$	—	—	13·0	—	—	13·3 *
p-CO_2H ‡	Pr^n	1	218—219	80	$C_{19}H_{16}O_4N_2$	66·9	5·4	8·4	67·5	5·3	8·3
,,	Bu^n	1	250—251 †	80	$C_{20}H_{20}O_4N_2$	67·4	5·4	7·7	68·2	5·7	8·0
p-AcO	Pr^n	2	140—141	53	$C_{22}H_{22}O_6N_2$	63·9	5·4	6·9	64·4	5·4	6·8
,,	Bu^n	2	180—181	53	$C_{23}H_{24}O_6N_2$	64·6	5·6	6·6	65·1	5·7	6·6
p-BzO	Pr^n	2	187—188 †	69	$C_{32}H_{26}O_6N_2$	71·7	4·8	5·2	71·9	4·9	5·2
,,	Bu^n	2	179—180 †	69	$C_{33}H_{28}O_6N_2$	72·0	5·1	5·0	72·3	5·1	5·1

* Found: Ac, 20·9—21·3. Required: Ac, 20·4%.
† Crystallised from glacial acetic acid; other products from ethanol.
‡ R = *p*-CO_2H; R′ = H.

n-Butylmalonyl Chloride.[18]—*n*-Butylmalonic acid (65 g.) was heated with thionyl chloride (100 ml.; purified according to Fieser, " Experiments on Organic Chemistry," Heath and Co., New York, 2nd edn., p. 381) for 48 hr. at 40—50° and then for 6 hr. at 60°. The product distilled over as colourless liquid, b. p. 88—92°/15 mm. (lit.,[21] 92—96°/22 mm.); yield 64 g. (75%).

n-Propylmalonyl chloride, similarly prepared, had b. p. 75—78°/15 mm.

[13] Cook and Jones, *J.*, 1939, 1310.
[14] Willstätter and Benz, *Ber.*, 1906, **39**, 3495; 1907, **40**, 1582.
[15] Anspon, *Org. Synth.*, 1945, **20**, 86.
[16] Angeli and Valori, *Atti R. Accad. Lincei*, 1913, **22**, 132.
[17] Werner and Stiasny, *Ber.*, 1899, **32**, 3272.
[18] Willgerodt, *J. prakt. Chem.*, 1890, **42**, 49.
[19] Khalifa and Linnell, *J. Org. Chem.*, in the press.
[20] Jacobson and Steinbrenk, *Annalen*, 1898, **303**, 384.
[21] Puterbaugh, Sivamer, and Hauser, *J. Amer. Chem. Soc.*, 1952, **74**, 3439.

3 : 5-*Dioxopyrazolidine Derivatives.*—(1) The hydrazo-compound, suspended in dry benzene, is heated with a slight excess of the acid chloride for 3 hr. at 70—80° with continuous stirring (mercury seal). Then the benzene and the excess of acid chloride are distilled off under vacuum, and the residue is extracted with sodium carbonate solution (charcoal). Acidification of the alkaline extract (Congo Red) with 5N-hydrochloric acid affords the pyrazolidine derivative.

(2) The hydrazo-compound, suspended in acetic anhydride (*ca.* 25 ml. per 1 g.), is heated with a slight excess of the acid chloride with continuous stirring (mercury seal) for 2 hr. at 50—60° under nitrogen and in the presence of a trace of zinc dust. The mixture is filtered from the zinc, most of the acetic anhydride and excess of acid chloride removed, and the residue refluxed with absolute alcohol for ½ hr. to esterify traces of the acid chloride and anhydride. (Extraction with aqueous sodium carbonate, as above, gave a product which could not be purified.) The alcoholic solution on concentration and cooling affords the pyrazolidine derivative. *Diacetamido pyrazolidine derivatives* (I; R = R′ = NHAc, R″ = Pr^n or Bu^n) were obtained by reducing the corresponding dinitro-derivatives with zinc dust and ammonium chloride [12] and acetylating the resulting diamino-derivatives.

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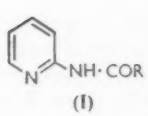
262. *Potentially Tautomeric Pyridines. Part II.*[1] 2-, 3-, *and* 4-*Acetamido- and -Benzamido-pyridine.*

By R. A. JONES and A. R. KATRITZKY.

The basicities and spectra of the compounds named in the title and alkylated derivatives of their alternative tautomers show that they exist predominantly in the acylamino-form; the reasons for this somewhat unexpected behaviour are discussed.

ACYLAMINO-GROUPS often show properties intermediate between those of free amino- and hydroxy-groups; *e.g.*, acidity and basicity and directive influence on electrophilic substitutions in benzenoid nuclei.[2] 2-, 3-, and 4-Aminopyridine exist as such,[3] but 2- and 4-hydroxypyridine exist as pyrid-2- and -4-one,[4] and 3-hydroxypyridine exists in comparable amounts as such and as anhydro-3-hydroxypyridinium hydroxide.[4] A knowledge of the tautomeric composition of 2- (I ⇌ II), 3- (III ⇌ IV), and 4-acylaminopyridines (cf. I ⇌ II) would therefore be of interest. Kenner, Reese, and Todd [5] showed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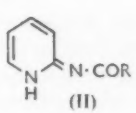
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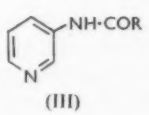
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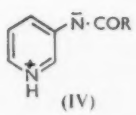
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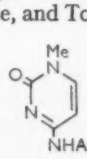
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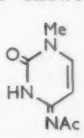

(VI)

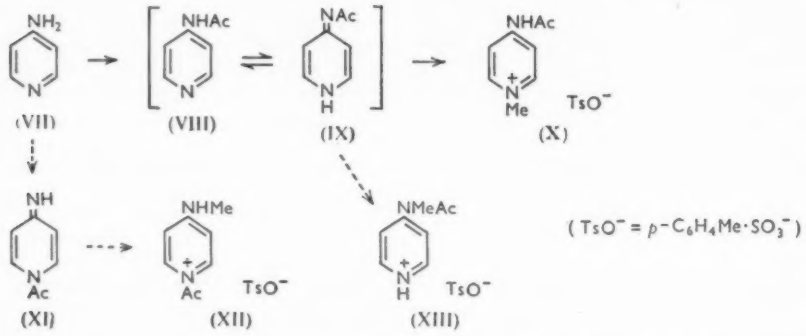
by ultraviolet-spectral comparisons that N^6-acetyl-3-methylcytosine exists predominantly as such (V) and not in the alternative form (VI); no other work has been reported. 2-, 3-, and 4-Acetamido- and -benzamido-pyridine and methylated derivatives of their alternative tautomers have now been prepared and studied by basicity and ultraviolet- and infrared-spectral techniques.[1,6]

Preparation of Compounds.—Hydrogenation of 4-methylaminopyridine 1-oxide gave

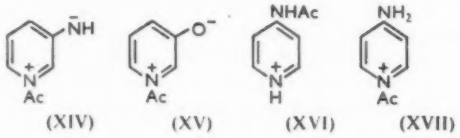
[1] Part I, Jones and Katritzky, *J.*, 1958, 3610.
[2] See, *e.g.*, Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 239.
[3] Angyal and Angyal, *J.*, 1952, 1461.
[4] Albert and Phillips, *J.*, 1956, 1294; Mason, *J.*, 1958, 674.
[5] Kenner, Reese, and Todd, *J.*, 1955, 855; cf. also Brown, Todd, and Varadarajan, *J.*, 1956, 2384.
[6] Gardner and Katritzky, *J.*, 1957, 4375.

4-methylaminopyridine (compare ref. 7). 2-[8] and 3-Methylamino-[9] and 4-amino-pyridine [7] were prepared by known methods. Monoacylation of these amines and (commercial) 2- and 3-aminopyridine (see p. 1322) yielded 2-, 3-, and 4-acetamido-, -benzamido-, -*N*-methylacetamido-, and -*N*-methylbenzamido-pyridine. The first six acylamino-compounds were heated with methyl toluene-*p*-sulphonate; 2-, 3-, and 4-acetamido- and 3- and 4-benzamido-1-methylpyridinium toluene-*p*-sulphonate were obtained, but no product could be isolated from the 2-benzamidopyridine reaction.

It was necessary to confirm the gross structures assigned to the above acylated products,



because, *e.g.*, acetylation of 4-aminopyridine (VII) could have given (XI) instead of an equilibrium mixture of (VIII) and (IX). The mixture of (VIII) and (IX) and methyl toluene-*p*-sulphonate could have given (XIII) instead of (X), and 1-acetylpyrid-4-one imine (XI) could have given (XII). The following facts show that acylation did not give (XI) or its analogues. (i) 2-[10,11] and 3-Acetamido-[12] and 2-benzamido-pyridine [10] with peracetic acid gave substituted pyridine 1-oxides, of known [12] structure. (ii) In the 3-series, the alternative structures are betaines, *e.g.*, (XIV), but the products' properties did not



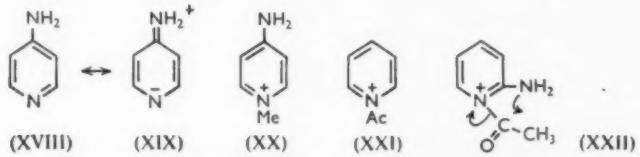
resemble those of known betaines (*e.g.*, XV).[13] (iii) The compounds were reasonably stable in dilute aqueous acid (no significant change in ultraviolet spectrum of a N-acid solution during 24 hr. for 2- and 4-acet- and -benz-amidopyridine), as would be expected for ions of type (XVI) (from VIII ⇌ IX) but not for ions of type (XVII) (from XI). (iv) Infrared spectra (see below) eliminate structures of types (XI) and (XIV).

Acylation of the nitrogen atom in the side chain rather than that in the ring is interesting, because the two principal canonical forms of 2- and 4-aminopyridine (*e.g.*, XVIII and XIX) and the net charge distribution should cause electrophilic agents to attack the ring-nitrogen atom. This generally happens; thus methylation gives compound (XX).[14] Initial acylation probably occurs on the ring-nitrogen atom, but the products

[7] Katritzky and Monro, *J.*, 1958, 1263.
[8] Anderson and Seeger, *J. Amer. Chem. Soc.*, 1949, **71**, 340.
[9] Clark-Lewis and Thompson, *J.*, 1957, 442.
[10] Katritzky, *J.*, 1957, 191.
[11] Adams and Miyano, *J. Amer. Chem. Soc.*, 1954, **76**, 2785.
[12] Jones and Katritzky, unpublished work.
[13] Williams, *J. Ind. Eng. Chem.*, 1921, **13**, 1107.
[14] Tschitschibabin and Ossetrowa, *Ber.*, 1925, **58**, 1708.

(*e.g.*, XVII) are acylating agents [cf., *e.g.*, the ion (XXI) formed during acylation in pyridine] and rearrange intermolecularly [and possibly intramolecularly, in the 2-series (*e.g.*, XXII)]. Angyal *et al.*[15] concluded that this occurred in the benzoylation and sulphonylation of 2-aminopyridine.

Methyl toluene-*p*-sulphonate did not give products of type (XIII), for the corresponding free bases were spectroscopically distinct from the (acyl-*N*-methylamino)-pyridines and had quite different basicities; the identity of the products from the



(XVIII) (XIX) (XX) (XXI) (XXII)

methylation of 2-benzamidopyridine and the benzoylation of 1-methylpyrid-2-one imine had been previously established.[16]

Basicity Measurements.—The pK_a values in Table 1 show that (*a*) the 2-, 3-, and 4-(acyl-*N*-methylamino)pyridines are weaker bases by 0·14—2·08 pK units, and (*b*) the 1-methylpyrid-2- and -4-one acylimines and the anhydro-3-acylamino-1-methylpyridinium

TABLE 1.

No.	Compound	pK_a [a]	σ [b]	Concn. (10^{-4}M)	Wavelength [c] (mμ)	pK_a of corresp. NH_2 cpd.[d]	pK_a of corresp. OH cpd.[d]
1	2-Acetamidopyridine	4·09	0·04	310	—	6·86	3·28 [e]
2	2-(*N*-Methylacetamido)pyridine	2·01	0·05	0·03	290	—	—
3	1-Methylpyrid-2-one acetylimine	7·12	0·06	96	—	12·2	0·32
4	2-Benzamidopyridine	3·33	0·08	310	—	6·86	3·28 [e]
5	2-(*N*-Methylbenzamido)pyridine	1·44	0·02	0·28	295	—	—
6	3-Acetamidopyridine	4·46	0·09	227	—	6·09	4·88 [e]
7	3-(*N*-Methylacetamido)pyridine	3·52	0·04	115	—	—	—
8	Anhydro-3-acetamido-1-methylpyridinium hydroxide	>11	—	—	—	—	4·96
9	3-Benzamidopyridine	3·80	0·06	1·95	280	6·09	4·88 [e]
10	3-(*N*-Methylbenzamido)pyridine	3·66	0·10	0·87	280	—	—
11	Anhydro-3-benzamido-1-methylpyridinium hydroxide	>11	—	—	—	—	4·96
12	4-Acetamidopyridine	5·87	0·03	180	—	9·17	6·62 [e]
13	4-(*N*-Methylacetamido)pyridine	4·62	0·03	130	—	—	—
14	1-Methylpyrid-4-one acetylimine	11·03	0·03	210	—	12·5	3·33
15	4-Benzamidopyridine	5·32	0·08	88	—	9·17	6·62 [e]
16	4-(*N*-Methylbenzamido)pyridine	4·68	0·01	127	—	—	—
17	1-Methylpyrid-4-one benzoylimine	9·89	0·07	135	—	12·5	3·33

[a] Arithmetical means of 6 values. Apparent values are given; thermodynamic pK_a may be calculated by using the concentration given (cf. ref. 4). [b] Standard deviation. [c] An entry in this column signifies that the determination was spectrometric (otherwise potentiometric). Measurements were made in phosphate buffers, or sulphuric acid of known H_0 and containing up to 2% of ethanol. [d] From refs. 3, 4, and Jaffe and Doak, *J. Amer. Chem. Soc.*, 1955, **77**, 4441. [e] These values refer to 2-, 3-, and 4-methoxypyridine. [f] Jaffe and Doak (*loc. cit.*) give 4·43.

hydroxides are stronger bases by ⩾3·03 pK units than the corresponding, potentially tautomeric compounds. Observation (*b*) demonstrates that 2-, 3-, and 4-acetamido- and -benzamido-pyridine exist predominantly as such (I and III), and not as pyridine acylimines or betaines (II and IV), if the reasonable assumption is made that a methyl group has only a weak base-strengthening effect.

Observation (*a*) indicates considerable steric inhibition of resonance in the (acyl-*N*-methylamino)-compounds. The differences are least in the 3-series, where mesomeric

[15] Angyal and his co-workers, *Austral. J. Sci. Res.*, 1951, **4**, *A*, 93; 1952, **5**, *A*, 368, 375.
[16] Tschitschibabin and Bylinkin, *Ber.*, 1922, **55**, 998.

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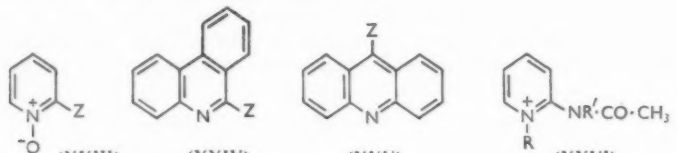
base-strengthening by the acylamino-group is of least importance, and greatest in the 2-series, where steric hindrance is most effective. The differences are smaller for the benzamido- than for the acetamido-compounds; possibly mesomerism in the former is considerably hindered before introduction of the methyl group. Similar effects are shown in alkylamino-compounds, *e.g.*, weak in the pyridine 1-oxides [6] (XXIII; Table 2, col. 1)

TABLE 2. pK_a *Values.*

Z	1	2	3
NH_2	2·67	6·30	9·45
NHMe	2·61	6·70	9·77
NMe_2	2·27	4·91	7·53

(For explanation see text.)

and strong in the phenanthridines [17] (XXIV; col. 2) and acridines [18] (XXV; col. 3). Steric inhibition of mesomerism in (*N*-methylacetamido)-compounds is also indicated by ultraviolet-spectral (see below) and kinetic evidence.[19]



(XXIII) (XXIV) (XXV) (XXVI)

Ultraviolet Spectra (*Table* 3).—Each series of compounds forms similar cations, *e.g.*, Nos. 1—3 form the cation (XXVI; R and R′ = H or Me). The positions of the ultraviolet absorption maxima are similar in each series of cations, but each (acyl-*N*-methylamino)-compound shows sharply reduced intensity of absorption compared with the other two compounds, indicating partial steric inhibition of mesomerism.[20]

In each series of free bases, the positions of the absorption maxima of the (acylamino)-compounds are similar to those of the (acyl-*N*-methylamino)-compounds and not to those of the pyridone acylimines or anhydro-bases. The lower intensities of the (acyl-*N*-methylamino)- than of the (acylamino)-compounds are explained by steric inhibition of mesomerism (cf. the cations). The ultraviolet spectra therefore afford independent evidence that the acylamino-forms of the potentially tautomeric compounds predominate.

Infrared Spectra.—For monosubstituted aromatic and heteroaromatic compounds, the bands are (with few exceptions) characteristic of either the ring or the substituent, and in a series of compounds containing the same ring (or substituent), the positions and intensities of the bands are either reasonably constant or vary in a regular manner with the nature of the substituent (or ring).[21-23] The bands characteristic of the substituted nuclei are shown by pyridines with the following substituents: 2- and 4-(*N*-methylacetamido)- and 4-(*N*-methylbenzamido)- (see p. 1323); and by 2-[21], 3-[22], and 4-acetamido-[23]; 3-(*N*-methylacetamido)-[22]; 2-[21], 3-[22], and 4-benzamido-,[23] and 2-[21] and 3-(*N*-methylbenzamido-;[23] the remaining bands are characteristic of the substituent.[12] Thus, in chloroform solution, the potentially tautomeric compounds all exist predominantly in the acylamino-form.

[17] Reese, *J.*, 1958, 898.
[18] Albert and Goldacre, *J.*, 1946, 706.
[19] de la Mare and Hassan, *J.*, 1958, 1519.
[20] See, *e.g.*, Ingraham in Newman, "Steric Effects in Organic Chemistry," Chapman and Hall, London, 1956, p. 481.
[21] Katritzky and Hands, *J.*, 1958, 2202.
[22] Katritzky, Hands, and Jones, *J.*, 1958, 3168.
[23] Katritzky and Gardner, *J.*, 1958, 2198.

TABLE 3.

Free bases [a]

No.	Compounds	$\lambda_{min.}$ mμ	$\lambda_{min.}$ $10^{-3}\varepsilon$	$\lambda_{max.}$ mμ	$\lambda_{max.}$ $10^{-3}\varepsilon$	$\lambda_{min.}$ mμ	$\lambda_{min.}$ $10^{-3}\varepsilon$	$\lambda_{max.}$ mμ	$\lambda_{max.}$ $10^{-3}\varepsilon$
1	2-Acetamidopyridine	213	5·0	232	10·1	252	3·2	273	7·0
2	2-(*N*-Methylacetamido)pyridine	212	4·8	224	5·3	248	3·0	262	4·1
3	1-Methylpyrid-2-one acetylimine [d]	243	5·0	265	5·4	278	4·2	311	7·4
4	2-Benzamidopyridine	219	7·2	242	11·8	260	9·9	278	12·9
5	2-(*N*-Methylbenzamido)pyridine	—		(—) [c]		253	6·2	269	7·1
6	3-Acetamidopyridine	214	4·0	236	9·8	262	3·0	271	3·1
7	3-(*N*-Methylacetamido)pyridine	—		230 *	4·7	248	3·4	260·5	3·6
8	Anhydro-3-acetamido-1-methylpyridinium hydroxide [d]	247	6·7	273	8·9	—		312 *	3·5
9	3-Benzamidopyridine	—		(—) [c]		216	10·8	258	15·8
10	3-(*N*-Methylbenzamido)pyridine	—		(—) [c]		235	13·8	262	15·7
11	Anhydro-3-benzamido-1-methylpyridinium hydroxide [d]	—		222	18·3	255	8·8	292	12·3
12	4-Acetamidopyridine	—		—		218	3·0	244	17·7
13	4-(*N*-Methylacetamido)pyridine	—		—		219	5·2	253	10·3
14	1-Methylpyrid-4-one acetylimine [d]	240	0·1	269	5·8	281	5·4	312	18·0
15	4-Benzamidopyridine	—		—		222	6·0	263	17·2
16	4-(*N*-Methylbenzamido)pyridine	—		—		234	8·4	260	13·2
17	1-Methylpyrid-4-one benzoylimine [d]	—		226	15·2	275	5·7	328	26·8

Ions [b]

No.	$\lambda_{max.}$ mμ	$\lambda_{max.}$ $10^{-3}\varepsilon$	$\lambda_{min.}$ mμ	$\lambda_{min.}$ $10^{-3}\varepsilon$	$\lambda_{max.}$ mμ	$\lambda_{max.}$ $10^{-3}\varepsilon$	$\lambda_{min.}$ mμ	$\lambda_{min.}$ $10^{-3}\varepsilon$	$\lambda_{max.}$ mμ	$\lambda_{max.}$ $10^{-3}\varepsilon$
1	—		212	4·5	229	12·2	246	0·6	291	11·8
2	—		215	3·0	235	8·3	254	1·1	293	7·7
3	—		215	5·8	229	9·8	248	0·9	290	9·8
4	—		219	6·8	244	14·3	265	4·9	297	20·5
5	—		219	8·7	239	10·1	265	5·0	296	11·3
6	212	19·9	229	5·3	247	11·0	266	2·5	287	5·3
7	223	8·7	245	5·3	250	5·5	275	4·0	280	4·2
8	218	19·0	226	3·8	249	11·2	269	3·1	290	5·3
9	226	13·9	238	12·7	259	20·5	—		280 *	13·9
10	223	12·3	247	8·3	258	8·7	—		285 *	6·0
11	227	18·0	241	11·3	261	18·3	—		288 *	8·9
12	—		—		206	12·3	222	1·5	266	20·0
13	—		206	7·0	214	8·4	230	1·2	281	14·2
14	—		—		212 *	11·4	225	2·4	272	22·0
15	—		—		(—) [c]		225	3·6	279	32·0
16	—		210	12·9	218	14·5	250	5·7	291	13·9
17	—		—		215	17·4	235	5·3	285	32·8

Solutions were aqueous, and phosphate buffers were used.
* Inflection.
[a] Nos. 3, 8, 11, 14, and 17 in N-sodium hydroxide, others at pH 9·7. [b] Nos. 2 and 5 in 5N-sulphuric acid, others in N-sulphuric acid. [c] Peak hidden by increasing absorption. [d] These compounds decompose on storage in N-sodium hydroxide, but the spectra were measured before this was appreciable.

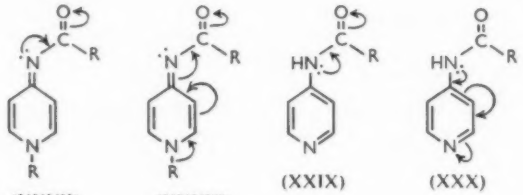
TABLE 4. *Log of parts of pyridine form present to one part of pyridone, etc., form.*

	OH [a]	NH_2 [a]	NHAc [a]	NHBz [a]	SH [b]
2-Substituted pyridine	−2·5	+5·3	+3·0	—	−4·5
3-Substituted pyridine	0	—	>6·5	>7·2	−2·5
4-Substituted pyridine	−3·3	+3·3	+5·2	+4·5	−4·0

All values refer to aqueous solutions.
[a] This work. [b] Ref. 1 and Albert, personal communication.

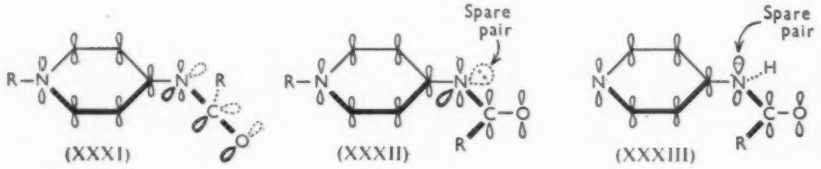
Discussion.—The equilibrium proportions of the alternative forms for the tautomeric pyridines studied are summarised in Table 4. From the discussion in the first paragraph of this paper, it would not be expected that the acylamino-, like the amino-, but unlike the hydroxy-, compounds exist overwhelmingly in the pyridine form. The basicities of the acylaminopyridines are closer to those of the methoxy- than to those of the amino-compounds (Table 1); the position of tautomeric equilibrium is determined by the base strength

of the pyridone acylimines, which are strong bases, like the pyridone imines but not the pyridones (Table 1). In other words, converting NH into N·COR decreases, relatively to the conversion of NH into O, the basicity of a pyridone form much less than that of a pyridine form. Therefore some new factor must be destabilising the pyridone acylimines relative to the acylaminopyridines. A probable explanation is that mesomerism of type (XXVII) [which requires the C=O π-orbital to be in the plane of the ring (cf. XXXI)] and mesomerism of type (XXVIII) [which requires the C=O π-orbital to be perpendicular to the ring (cf. XXXII)] cannot occur simultaneously; on the other hand, overlap of the



(XXVII) (XXVIII) (XXIX) (XXX)

nitrogen spare pair of electrons with both the ring (XXIX) and the carbonyl orbitals (XXX) at the same time is possible (cf. XXXIII).



(XXXI) (XXXII) (XXXIII)

Experimental

2-Acetamido-1-methylpyridinium Toluene-p-sulphonate.—2-Acetamidopyridine (m. p. 68—69°; lit.,[24] m. p. 71°) (0·25 g.) and methyl toluene-*p*-sulphonate (0·28 g.), heated for 12 hr. at 105°, gave the *toluene-p-sulphonate* (0·33 g., 62%) which separated from ethanol–ethyl acetate (1 : 6) in needles, m. p. 113—114° (Found: C, 55·5; H, 5·7; N, 8·5. $C_{15}H_{16}O_4N_2S$ requires C, 55·8; H, 5·6; N, 8·7%).

2-Benzamidopyridine (m. p. 79—80°; lit.,[25] m. p. 79—81°) appeared to decompose when heated with methyl toluene-*p*-sulphonate.

2-(N-Methylacetamido)pyridine.—2-(Methylamino)pyridine (1 g.), acetic acid (2 c.c.), and acetic anhydride (2 c.c.) were refluxed for 2 hr. Volatile material was removed at 100°/20 mm.; distillation of the residue gave the *pyridine* (0·75 g., 54%), b. p. 74—75°/0·2 mm., n_D^{17} 1·540 (Found: N, 18·7. $C_8H_{10}ON_2$ requires N, 18·7%). Infrared bands due to the 2-pyridine nucleus[21] were: 2990 (50), 1594 (210), 1578* (110), 1471 (180), 1434 (155), 1285* (60), 1140† (90), 1090† (90), 1045 (25), 990 (30).‡ The *picrate* formed needles (from ethanol), m. p. 189·5—190·5° (Found: N, 19·0. $C_{14}H_{13}O_8N_5$ requires N, 18·5%).

2-(*N*-Methylbenzamido)pyridine[26] had m. p. 60—63° (lit.,[26] m. p. 61—62°).

4-Acetamido-1-methylpyridinium Toluene-p-sulphonate.—Acetylation[24] of the amine gave 4-acetamidopyridine (92%); the hydrate, m. p. 121—123° (lit.,[24] m. p. 124°), separated from water. The anhydrous salt crystallised from chloroform in rods, m. p. 148°, (lit.,[24] m. p. 150°).

* Shoulder. † Absorption considered to be due to two peaks overlapping. ‡ Values in parentheses are apparent extinction coefficients (cf. refs. 21—23).

[24] Camps, *Arch. Pharm.*, 1902, **240**, 345.
[25] Huntress and Walter, *J. Org. Chem.*, 1948, **13**, 735.
[26] Tschitschibabin and Khunjanz, *Ber.*, 1928, **61**, 2215.

Treatment as above gave the *toluene*-p-*sulphonate* (85%), which separated from ethanol–ethyl acetate (1 : 5) in deliquescent needles, m. p. 135—137° (Found: C, 55·5; H, 5·4; N, 8·3%).

4-*Benzamido*-1-*methylpyridinium Toluene*-p-*sulphonate*.—4-Aminopyridine (0·5 g.), pyridine (3 c.c.), and benzoyl chloride (0·75 c.c.) were kept for 12 hr. at room temperature; addition of water then precipitated 4-benzamidopyridine (0·82 g., 80%), m. p. 203—204° after recrystallisation from water (lit.,[27] m. p. 202°).

Prepared as above, the *toluene*-p-*sulphonate* (91%) separated from ethanol–ethyl acetate (1 : 5) as deliquescent needles, m. p. 165—165·5° (Found: C, 62·5; H, 5·3; N, 6·9. $C_{20}H_{20}O_4N_2S$ requires C, 62·5; H, 5·2; N, 7·3%).

4-*Methylaminopyridine*.—4-Methylaminopyridine 1-oxide (1·9 g.) in ethanol (20 c.c.) was hydrogenated over 5% palladium–charcoal (0·5 g.) until uptake (initially *ca.* 150 c.c./hr.) ceased (*ca.* 3 hr.). Filtration, evaporation of the filtrate, and recrystallisation of the residue from benzene gave the pyridine (1·35 g., 82%), m. p. 119—120° (lit.,[14] m. p. 115—118°).

4-Methylaminopyridine (0·5 g.), acetic anhydride (1 c.c.), and acetic acid (1 c.c.) were refluxed for 2 hr. Volatile material was removed at 100°/20 mm., and the residue, in chloroform (10 c.c), digested with potassium carbonate (0·5 g.). Evaporation of the filtrate gave 4-(N-*methylacetamido*)*pyridine* (0·36 g., 52%), which separated from light petroleum in rods, m. p. 56—57° (Found: C, 63·3; H, 6·6; N, 18·7. $C_8H_{10}ON_2$ requires C, 63·9; H, 6·7; N, 18·7%). Infrared bands due to the 4-substituted pyridine nucleus[23] were: 2980 (60), 1596 (350), 1565 (65), 1495 (80), 1412 (75), 1061 (20), 997 (85), 830 (65).

4-Methylaminopyridine (0·5 g.), pyridine (0·5 c.c.), and benzoyl chloride (0·6 c.c.) were kept for 15 hr. at room temperature; 4-(N-*methylbenzamido*)*pyridine hydrochloride* (1·0 g., 86%) separated; it crystallised from ethanol–ethyl acetate (1 : 2) as plates, m. p. 189—190° (Found: C, 62·8; H, 5·3; N, 11·6. $C_{13}H_{13}ON_2Cl$ requires C, 62·7; H, 5·3; N, 11·3%). The salt (0·2 g.) was warmed with 2N-aqueous potassium hydrogen carbonate (2 c.c.) and extracted with ether; concentration of the extracts gave the *base* (0·12 g., 70%), which sublimed in needles, m. p. 85—86° (Found: C, 73·6; H, 6·0; N, 12·9. $C_{13}H_{12}ON_2$ requires C, 73·6; H, 5·7; N, 13·1%). Infrared bands due to the 4-substituted pyridine nucleus[23] were: 2950 (70), 1594 (320), 1563 (125), 1495 (120), 1415 (80), 1061 (15), 994 (shoulder) (25), 825 (95).

3-*Acylaminopyridine Derivatives*.—3-Acetamidopyridine had m. p. 132—133° (lit.,[28] m. p. 131°).

The following 3-substituted pyridines were prepared analogously to 4-benzamidopyridine: *benzamido* (67%), needles, m. p. 110—112°, from water (Found: C, 72·6; H, 4·9; N, 14·1. $C_{12}H_{10}ON_2$ requires C, 72·7; H, 5·1; N, 14·1%); N-*methylbenzamido* (37%), cubes, m. p. 92—93°, from light petroleum (Found: C, 73·8; H, 6·0. $C_{13}H_{12}ON_2$ requires C, 73·6; H, 5·7%).

Prepared similarly to the 4-isomer, 3-(*N*-methylacetamido)pyridine (35%) crystallised from light petroleum as plates, m. p. 62—64° (lit.,[29] m. p. 64°).

The following were prepared as the 2-isomers: 3-*acetamido*-1-*methyl*- (61%), needles (from ethanol–ethyl acetate), m. p. 149—150° (Found: C, 55·8; H, 5·8; N, 9·0. $C_{15}H_{18}O_4N_2S$ requires C, 55·9; H, 5·6; N, 8·7%), and 3-*benzamido*-1-*methylpyridinium toluene*-p-*sulphonate* (80%), needles (from ethanol), m. p. 178—179° (Found: C, 62·7; H, 5·3; N, 7·4. $C_{20}H_{20}O_4N_2S$ requires C, 62·5; H, 5·2; N, 7·3%).

Measurement of Spectra.—See Ref. 1 for details.

We thank Sir Alexander Todd, F.R.S., for his interest in this work which was carried out in part during the tenure (by A. R. K.) of an I.C.I. Fellowship.

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[27] Koenigs, Kinne, and Weiss, *Ber.*, 1924, **57**, 1176.
[28] Pictet and Crepieux, *Ber.*, 1895, **28**, 1908.
[29] Plazek, Marcinikow, and Stammer, *Rocznichi Chem.*, 1935, **15**, 365.

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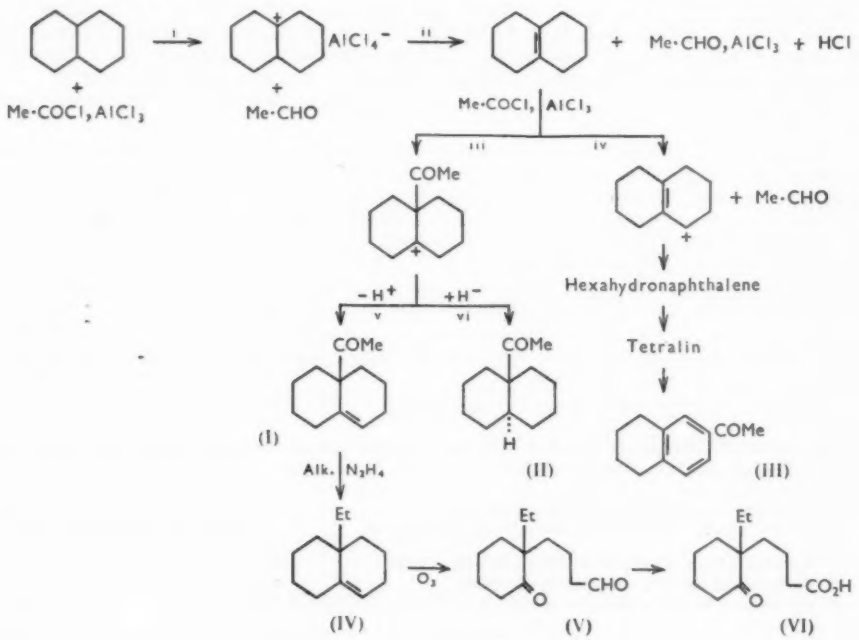
263. *The Interaction of Decalin and Friedel–Crafts Acetylating Agent.*

By G. Baddeley and E. Wrench.

In methylene or ethylene chloride at room temperature, and in the presence of excess of aluminium chloride, decalin and acetyl chloride provide 9-acetyl-*trans*-decalin, 10-acetyl-$\Delta^{1:9}$-octahydronaphthalene, 6-acetyltetralin, and a hydroxy-ketone $C_{12}H_{20}O_2$, m. p. 107—108°, which will be discussed in a further communication. These compounds are obtained also by interaction of $\Delta^{9:10}$-octalin and the acetylating agent.

Decalin readily reacts with the acetyl chloride–aluminium chloride complex at room temperature; the best yields of 10-acetyl-$\Delta^{1:9}$-octahydronaphthalene (I) and 9-acetyl-*trans*-decalin (II) were obtained when a mixture of decalin (3·6 moles), aluminium chloride (6 moles), acetyl chloride (4 moles), and methylene chloride (700 c.c.) was kept at room temperature for two days and then added to water. Fractional distillation gave a mixture of ketones (I) and (II), b. p. 120—125°/15 mm., in 50% yield, and 6-acetyltetralin (III), b. p. 130—135°/15 mm., in 22% yield. Ketone (III) was identified by its 2 : 4-dinitrophenylhydrazone and semicarbazone, and by oxidation to tetralin-6-carboxylic acid. Separation of ketones (I) and (II) was facilitated by the fact that, the carbonyl group of the former being less hindered sterically, the former provides a semicarbazone under



conditions which leave the latter unchanged. Thus the mixture was shown to consist of (I) 75% and (II) 25%.

Identifications.—Oxidation of 9-acetyl-*trans*-decalin (II), first with selenium dioxide and then with alkaline hydrogen peroxide, gave *trans*-decalin-9-carboxylic acid, m. p.

134°. This acid contained no terminal methyl group and was dehydrogenated to naphthalene, and its acid chloride, like other tertiary acid chlorides, evolved carbon monoxide when added to a mixture of benzene and aluminium chloride. The other product was a hydrocarbon $C_6H_5{\cdot}C_{10}H_{17}$. Catalytic hydrogenation of 10-acetyl-$\Delta^{1:9}$-octahydronaphthalene gave 9-acetyl-*trans*-decalin: identification of the octahydro-compound involved reduction by lithium aluminium hydride to the corresponding secondary alcohol and preparation of its α-naphthylurethane, m. p. 162°. Wolff–Kishner reduction of the octahydro-ketone (I) gave the hydrocarbon (IV) from which the keto-aldehyde (V) was obtained by ozonolysis and the keto-acid (VI) by further oxidation with alkaline hydrogen peroxide.

In the annexed scheme, which is now proposed, reaction (i) involves transfer of hydride ion from a decalin molecule to an acetyl cation and together with step (ii) gives acetaldehyde, hydrogen chloride, and 9 : 10-octalin. This octalin was not isolated, but it is presumably an intermediate since, when added to the acetylating agent, it gave a mixture of ketones (I), (II), and (III). Apparently, 9 : 10-octalin can be dehydrogenated [reaction (iv)] to tetralin which is acetylated, or it can combine with an acyl cation [reaction (iii)], forming a carbonium ion which can give the product (I) by losing a proton [reaction (v)] or the product (II) by gaining a hydride ion [reaction (vi)].

The products of interaction of decalin and the Friedel–Crafts acetylating agent in the presence of excess of acetyl chloride are different from those of interaction in the presence of excess of aluminium chloride and throw light on the course of the interaction. Further discussion of the mechanism is therefore postponed.

Experimental

Interaction of Decalin, Acetyl Chloride, and Aluminium Chloride.—After many experiments the following procedure was found to give the highest yields of the required fraction, b. p. 120—125°/15 mm. A mixture of decalin (500 g.), anhydrous aluminium chloride (840 g.), acetyl chloride (320 g.) and methylene chloride (700 c.c.) was kept at room temperature for 2 days and then poured on ice and dilute hydrochloric acid. The methylene chloride layer was separated, dried (K_2CO_3), and distilled, and gave a fraction (259 g.), b. p. 118—135°/15 mm. Repeated fractional distillation gave fractions (i) (175 g.), b. p. 120—125°/15 mm., and (ii) (75 g.), b. p. 130—135°/15 mm. The latter was mainly 6-acetyltetralin: it gave a 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 235° (Found: C, 60·9; H, 5·4; N, 16·6. Calc. for $C_{18}H_{18}O_4N_4$: C, 61·2; H, 5·1; N, 15·8%), a semicarbazone, m. p. and mixed m. p. 236° (Found: C, 67·5; H, 7·3; N, 18·3. Calc. for $C_{13}H_{17}ON_3$: C, 67·5; H, 7·4; N, 18·2%), and, by hypochlorite oxidation, tetralin-6-carboxylic acid, m. p. and mixed m. p. 153° (Found: C, 75·4; H, 6·7%; equiv., 172. Calc. for $C_{11}H_{12}O_2$: C, 75·0; H, 6·8%; equiv., 176). Fraction (i) very slowly deposited a solid *substance* (*ca.* 5 g.) which crystallized from light petroleum in needles, m. p. 107—108° (Found: C, 73·5; H, 10·2. $C_{12}H_{20}O_2$ requires C, 73·6; H, 10·2%), gave a 2 : 4-dinitrophenylhydrazone, a *semicarbazone*, m. p. 238° (Found: C, 61·2; H, 9·1; N, 16·6. $C_{13}H_{23}O_2N_3$ requires C, 61·6; H, 9·1; N, 16·6%), and an *α-naphthylurethane*, m. p. 162° (Found: C, 75·9; H, 7·3; N, 3·9. $C_{23}H_{27}O_2N$ requires C, 75·6; H, 7·4; N, 3·8%). Fraction (i) (47 g.), semicarbazide hydrochloride (74 g.), and potassium acetate (94 g.) in water (280 c.c.) and ethanol (235 c.c.) were refluxed for 2 hr. A small precipitate, m. p. 270° (decomp.) (Found: C, 19·7; H, 4·9; N, 41·8%), was separated and discarded and the filtrate was poured into water (1 l.). The oily precipitate thus obtained was isolated and, by extraction with boiling light petroleum, separated into a *semicarbazone*, m. p. 254° (45 g.) after recrystallisation from dilute ethanol (Found: C, 66·3; H, 8·9; N, 17·4. $C_{13}H_{21}ON_3$ requires C, 66·3; H, 8·9; N, 17·9%), and an oil (11 g.), b. p. 122—125°/15 mm. (Found: C, 80·4; H, 11·3. $C_{12}H_{20}O$ requires C, 80·0; H, 11·1%).

Identification of the oil. It was shown to be 9-*acetyl*-trans-*decalin*. It did not decolorise bromine in carbon tetrachloride or aqueous potassium permanganate solution. A mixture of the oil (7·2 g.) and lithium aluminium hydride (3·2 g.) in dry ether (125 c.c.) was refluxed for 3 hr. and poured on ice and dilute sulphuric acid; the ethereal layer was separated, dried (K_2CO_3), and distilled, and gave 9-1′-*hydroxyethyldecalin* (*ca.* 7 g.), b. p. 136—138°/15 mm. (Found:

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C, 79·2; H, 11·9. $C_{12}H_{22}O$ requires C, 79·1; H, 12·1%), which formed an *α-naphthylurethane* which crystallised from ligroin in prisms, m. p. 162° (Found: C, 78·95; H, 8·1; N, 3·9. $C_{23}H_{29}O_2N$ requires C, 78·6; H, 8·3; N, 4·0%).

A mixture of the oil (2 g.) and selenium dioxide (1 g.) in dioxan (35 c.c.) and water (0·5 c.c.) was refluxed for 4 hr. It was freed from selenium by filtration, poured into water (100 c.c.), and extracted with chloroform (3 × 30 c.c.). The extracts were dried (Na_2SO_4), the solvent was removed, and the residue, in ethanol (100 c.c.), was treated with hydrogen peroxide (100-vol.; 10 c.c.) and 8% sodium hydroxide solution (15 c.c.) at 70° for 30 min. Removal of ethanol by distillation, and acidification of the residue, gave an oil which was extracted with ether (2 × 20 c.c.). Acidification of sodium hydrogen carbonate extracts of the ethereal solution gave prisms, m. p. 132—134° after recrystallisation from light petroleum (Found: C, 73·0; H, 9·5%; equiv., 170. Calc. for $C_{11}H_{18}O_2$: C, 72·5; H, 9·9%; equiv., 180), of *trans*-decalin-9-carboxylic acid (Dauben, Tweit, and Maclean [1] report m. p. 133—134°).

This acid (10 g.) was refluxed with thionyl chloride (30 c.c.) for 1 hr. Distillation of the product gave the acid chloride (8 g.), b. p. 115—118°/15 mm. This chloride in benzene (10 c.c.) was gradually added with stirring to a suspension of finely powdered aluminium chloride (6 g.) in benzene (30 c.c.). A vigorous reaction with evolution of hydrogen chloride and carbon monoxide ensued and the conventional working up gave an oil, b. p. 158—164°/15 mm., which was added to a mixture of acetyl chloride (2 g.) and aluminium chloride (3 g.) in methylene chloride (10 c.c.). The resulting acetyl derivative gave a *semicarbazone*, m. p. 196° (Found: C, 72·5; H, 8·4; N, 13·2. $C_{19}H_{27}ON_3$ requires C, 72·8; H, 8·6; N, 13·4%), and, therefore, was the product of acetylation of a hydrocarbon $C_6H_5{\cdot}C_{10}H_{17}$.

A mixture of the acid (0·5 g.) and 10% palladium–charcoal (0·5 g.) was heated at 220—240° for 48 hr. Carbon dioxide was liberated at 100°, and hydrogen (354 c.c. at 20°) was subsequently evolved. Naphthalene, m. p. and mixed m. p. 80°, condensed on the cooling thimble and gave a picrate of m. p. and mixed m. p. 149°.

Identification of the semicarbazone, m. p. 254°. Its hydrolysis with phthalic acid gave an oil, b. p. 120—122°/15 mm., in quantitative yield (Found: C, 80·4; H, 10·4. $C_{12}H_{18}O$ requires C, 80·9; H, 10·1%), which was 10-*acetyl*-$\Delta^{1:9}$-*octalin*. Over palladium–charcoal at room temperature it absorbed 1 mol. of hydrogen and gave a saturated ketone which did not give a semicarbazone but was reduced by ethereal lithium aluminium hydride to 9-1′-hydroxyethyl-*trans*-decalin, b. p. 136—138°/15 mm. (Found: C, 79·2; H, 11·9. Calc. for $C_{12}H_{22}O$: C, 79·1; H, 12·1%), which gave an α-naphthylurethane, m. p. and mixed m. p. 162°. Reduction of the unsaturated ketone by lithium aluminium hydride gave 10-1′-*hydroxyethyl*-$\Delta^{1:9}$-*octalin*, b. p. 135—136°/15 mm. (Found: C, 79·5; H, 11·1. $C_{12}H_{20}O$ requires C, 80·0; H, 11·1%) [*α-naphthylurethane*, m. p. 136° (Found: C, 79·3; H, 7·6; N, 4·3. $C_{23}H_{27}O_2N$ requires C, 79·1; H, 7·7; N, 4·0%)].

The unsaturated ketone (25 g.), 85% hydrazine hydrate solution (37·5 c.c.), and potassium hydroxide (52·5 g.) in diethylene glycol (375 g.) were refluxed for 4 hr. and gave a product (16 g.), b. p. 90—95°/15 mm., which did not form a semicarbazone or 2 : 4-dinitrophenylhydrazone and decolorised only 50% of the amount of bromine (in carbon tetrachloride) calculated for 10-ethyl-$\Delta^{1:9}$octalin.

Ozone was passed through a solution of the product (4·5 g.) in water (3 c.c.) and glacial acetic acid (12 c.c.) at 0° for 2·5 hr., and gave 4-(1-ethyl-2-oxo*cyclo*hexyl)butanal (V) as an oil (2 g.) which afforded an orange-yellow *bis*-2 : 4-*dinitrophenylhydrazone*, m. p. 184° (Found: C, 51·4; H, 5·0; N, 19·7. $C_{24}H_{28}O_8N_8$ requires C, 51·8; H, 5·0; N, 20·1%).

Ozone was passed through another sample of the product (2 g.) in ethyl acetate (10 c.c.) for 1·5 hr. and gave an oil, b. p. >80°/15 mm., which was added to a mixture of 2N-sodium hydroxide (8 c.c.) and Merck's " Perhydrol " (15 c.c.); the mixture was warmed until the evolution of oxygen was complete. The alkali-soluble 4-(1-ethyl-2-oxo*cyclo*hexyl)butanoic acid was precipitated by addition of concentrated hydrochloric acid as an oil which gave an orange 2 : 4-*dinitrophenylhydrazone*, m. p. 215° (Found: C, 55·0; H, 6·3; N, 14·5. $C_{18}H_{24}O_6N_4$ requires C, 55·1; H, 6·1; N, 14·3%).

Interaction of $\Delta^{9:10}$-*Octalin, Acetyl Chloride, and Aluminium Chloride.*—The octalin (8·4 g.) in methylene chloride (20 c.c.) was slowly added to a cooled mixture of aluminium chloride (9 g.) and acetyl chloride (10 g.) in methylene chloride (20 c.c.); there was a vigorous reaction with evolution of hydrogen chloride. After 10 min., the mixture was worked up in the usual way and gave the same products as were obtained from decalin, *i.e.*, the hydroxy-ketone,

[1] Dauben, Tweit, and Maclean, *J. Amer. Chem. Soc.*, 1955, **77**, 48.

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$C_{12}H_{20}O_2$, m. p. and mixed m. p. 107—108°, 10-acetyl-$\Delta^{1:9}$-octalin (semicarbazone, m. p. and mixed m. p. 254°), 9-acetyl-*trans*-decalin [identified by the α-naphthylurethane (m. p. and mixed m. p. 162°) of the alcohol obtained by lithium aluminium hydride], and 6-acetyltetralin (semicarbazone, m. p. and mixed m. p. 236°).

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264. *The Second (Rapid) Step in the Nucleophilic Substitution of Alkyl Halides. Part I. Hydrolysis of Triphenylmethyl Chloride in Acetone of Low Water Content.*

By D. GOLOMB.

The hydrolysis of triphenylmethyl chloride in acetone of low water content follows the first-order kinetic law strictly. At first sight this appears to contradict the S_N1 scheme proposed by Hughes, Ingold, and their co-workers in which deviation from first-order kinetics is expected owing to accumulation of chloride ion. These ions will increase the reverse reaction of step (*a*) in: (*a*) $Ph_3C{\cdot}Cl \rightleftharpoons Ph_3C^+ + Cl^-$; (*b*) $Ph_3C^+ + H_2O \longrightarrow Ph_3C{\cdot}OH + H^+$. It was shown conductometrically that hydrochloric acid dissociates only slightly in acetone of low water content (K_a in water–acetone (3%—97%) 29·5° $\cong 2 \times 10^{-4}$); hence the increase of the reassociation in step (*a*) is almost negligible and no deviation from first-order kinetics is observed. On the other hand, addition of lithium chloride (a salt with a common ion) causes a large decrease in the first-order rate constant. It was shown that the dissociation of this salt is about 8 times that of hydrochloric acid; hence larger chloride-ion concentrations are present upon addition of lithium chloride, which retard hydrolysis.

Various additives and the ionizing power of the solvent affect differently the rates of the reactions in the above scheme. Perchloric acid and lithium perchlorate retard the reverse reaction in step (*a*) because of the primary salt effect and, therefore, increase the overall rate of hydrolysis. Silver nitrate diminishes the chloride concentration, thus accelerating the overall hydrolysis. Increase of the water content in acetone raises its ionizing power and enhances the dissociation in step (*a*). In heavy water the rate constant is depressed. Phenol has no marked consequences.

BATEMAN, CHURCH, HUGHES, INGOLD, and TAHER [1] discussed extensively the hydrolysis of the derivatives of diphenylmethyl halides in aqueous acetone in terms of the S_N1 scheme:

$$RX \underset{k_2}{\overset{k_1}{\rightleftharpoons}} R^+ + X^-; \quad R^+ + H_2O \xrightarrow{k_3} ROH + H^+$$

The detailed rate equation of this scheme, account being taken of the mass-law effect and ionic-strength effect as derived by Bateman *et al.*, is:

$$-\frac{d[RX]}{dt} = \frac{k_1^0[RX]}{\alpha^0[X^-]\ \text{antilog}\ (AI^{\frac{1}{2}}) + \text{antilog}\ (B\sigma I)} \quad . \quad . \quad . \quad . \quad (1)$$

where $A = -1{\cdot}815 \times 10^6(DT)^{-3/2}$; $B = -0{\cdot}912 \times 10^{16}(DT)^{-2}$; I = ionic strength; D is the dielectric constant of the solvent; k_1^0 is the rate constant of the dissociation of the carbon–halogen bond; $\alpha^0 = k_2^0/k_3^0$, where k_2^0 is the rate constant of the reaction between the carbonium ion and the halide and k_3^0 is the rate constant of the nucleophilic attack of a water molecule on the carbonium ion, all at zero ionic strength. k_2 and k_3 represent the rate constants of the fast steps in the nucleophilic substitution reactions. σ is a

[1] Bateman, Church, Hughes, Ingold and Taher, *J.*, 1940, 979.

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characteristic constant for each compound and equals z^2d, where z is the charge on the poles of the transition state in the dissociation step, and d is the distance between them.

Equation (1) was obtained by assuming that the reaction between the carbonium ion and water occurs with one of the water molecules of the hydration shell which surrounds the carbonium ion. No activation is needed for the reaction: the hydration shell simply "collapses." This hypothesis caused considerable criticism,[2,3] and the analyses of products in competitive substitution (following paper) do not confirm it. It seems that reaction of a carbonium ion with water requires some activation, and the water molecule may come from the bulk of the solution. In that case we have an activated ion–dipole interaction, whose rate is affected by the ionic strength according to:

$$\log k_3 = \log k_3^0 + CI \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where k_3 and k_3^0 are the rate constants at I and zero ionic strength respectively. C is given by:

$$C = \frac{8\pi \boldsymbol{N}e^3 \mu z \cos\theta}{2{\cdot}303\,(\boldsymbol{k}DT)^2}$$

where z is the charge of the reacting ion, μ is the dipole moment, and θ is the angle of approach of the ion to the axis of the dipole.[4]

For the carbonium ion–water interaction $z = 1$, $\mu = 1{\cdot}85$ D, and θ may have any value from 90° to 0°, thus varying the cosine from 0 to 1. Therefore the maximum value of C is $7 \times 10^7/(DT)^2$.

Introducing eqn. (2) into eqn. (1) together with the ionic-strength corrections for k_1 and k_2 as calculated by Bateman *et al.*, we obtain the following kinetic expression:

$$-\frac{\mathrm{d}[\mathrm{RX}]}{\mathrm{d}t} = \frac{k_1^0[\mathrm{RX}]}{\alpha^0[\mathrm{X}^-]\ \mathrm{antilog}\,(AI^{\frac{1}{2}} - CI) + \mathrm{antilog}\,(B\sigma I)} \quad . \quad . \quad . \quad (3)$$

If the only electrolytes present are the hydrohalic acid liberated in the hydrolysis and a univalent salt with a common ion to the acid, then

$$I = 1/2 \sum c_i z_i^2 = [\mathrm{X}^-]$$

In most organic solvents the electrolytes do not dissociate completely, and the concentration of the free $[\mathrm{X}^-]$ ions have to be estimated independently from conductance or potentiometric measurements. It will be shown that their concentration is very small in acetone of low water content, so the antilogarithmic factors containing I in the first power are close to unity. Accordingly eqn. (3) is reduced to:

$$-\frac{\mathrm{d}[\mathrm{RX}]}{\mathrm{d}t} = \frac{k_1^0[\mathrm{RX}]}{\alpha^0[\mathrm{X}^-]\ \mathrm{antilog}\,(AI^{\frac{1}{2}}) + 1} \quad . \quad . \quad . \quad . \quad . \quad (4)$$

i.e., the only reaction whose rate is markedly influenced by low concentrations of free ions is the reassociation step (k_2). For this reaction A is negative, so antilog $(AI^{\frac{1}{2}})$ is fractional and $\alpha^0[\mathrm{X}^-]$ is diminished, *i.e.*, the ionic-strength effect counteracts the mass-law effect.

The kinetics of the hydrolysis of triphenylmethyl chloride in acetone of low water content can be interpreted fairly well with the aid of eqn. (4). At higher water contents, where electrolytes are more dissociated, eqn. (3) should be applied. Unfortunately, in such media rates become too fast to be measured by ordinary means.

Experimental

Materials.—Triphenylmethyl chloride, obtained from the alcohol by refluxing it with acetyl chloride in benzene,[5] had m. p. 112°. Acetone was purified by refluxing a commercial grade

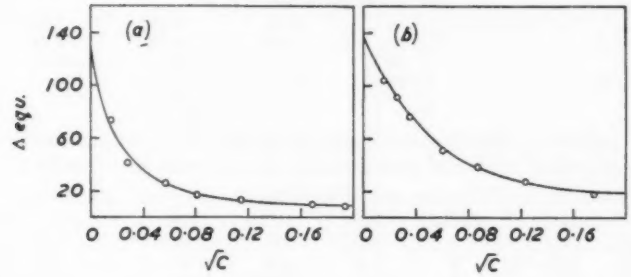
[2] Nash and Monk, *J.*, 1955, 1899.
[3] Spieth and Olson, *J. Amer. Chem. Soc.*, 1955, **77**, 1412.
[4] Moelwyn-Hughes, "Kinetics of Reaction in Solution," Oxford Univ. Press, 1947, p. 132.
[5] *Org. Synth.*, Coll. Vol. III, p. 839.

over solid potassium hydroxide–potassium permanganate, drying it twice over " Drierite " [$CaSO_4$], each time for 24 hr. with occasional shaking, and distilling it through a column. 0·05M-Triphenylmethyl chloride in such acetone gave about 0·02M-hydrochloric acid before any water was added, presumably owing to the water left. Lucchesi [6] showed by infrared spectrometry that traces of water are usually present in acetone, even if purified by recrystallization of its addition compound with sodium iodide. Hudson and Saville [7] dried acetone over phosphoric oxide, yet it contained 0·05% of water (0·03M).

Apparatus and Kinetic Measurement.—The rate was followed by measuring conductometrically the hydrochloric acid liberated in the reaction: $Ph_3C{\cdot}Cl + H_2O \longrightarrow Ph_3C{\cdot}OH + HCl$. The apparatus was described by Archer and Hudson.[8] A conductance cell (cell constant = 0·65) containing triphenylmethyl chloride in dry acetone was kept in a thermostat until constant temperature was reached. A measured volume of water at the same temperature was quickly introduced with a syringe pipette while the solution was stirred by a magnetic stirrer. The decrease in resistance as a function of time was measured. Zero time reading could be taken usually 10—20 seconds after mixing.

Resistance readings were calibrated against hydrochloric acid concentrations for every acetone–water mixture employed and also in presence of added substances. Even at the

FIG. 1. *Equivalent conductances of* (*a*) *hydrochloric acid and* (*b*) *lithium chloride in acetone containing 3% of water.*



lowest water content (1%), the water concentration was more than ten times that of the triphenylmethyl chloride concentration, so the reaction should be at least pseudo-unimolecular, represented by:

$$\bar{k}t = \log (c_\infty - c_0)/(c_\infty - c_t) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

where c_∞, c_0, and c_t are hydrochloric acid concentrations, and $\bar{k}$ is the observed rate constant. At very low water concentrations only part of the chloride hydrolyses and hence the rate constants obtained from eqn. (5) were multiplied by the fraction of reaction at equilibrium to obtain rate constants of the forward reaction (k). These fractions (% reaction) appear in Table 3.

Plots of eqn. (5) were always very good straight lines up to 2—3 half-times of reaction and $\bar{k}$ was obtained from the slopes.

For the evaluation of the mass-law and ionic-strength effects (cf. Discussion), dissociation constants of HCl and LiCl in acetone with 3% of water at 29·5° were estimated from conductance curves at high dilutions by Fuoss's graphical successive-approximation method.[9] The dielectric constant of this mixture [10] is 20 and the viscosity [11] is 33×10^{-4} cP. Plots of equivalent conductance are given in Fig. 1. The estimated dissociation constants are:

$$K_{HCl} = [H^+][Cl^-]/[HCl] = 1{\cdot}8 \times 10^{-4}; \quad K_{LiCl} = [Li^+][Cl^-]/[LiCl] = 1{\cdot}4 \times 10^{-3}$$

[6] Lucchesi, *J. Amer. Chem. Soc.*, 1956, **78**, 4229.
[7] Hudson and Saville, *J.*, 1955, 4130.
[8] Archer and Hudson, *J.*, 1950, 3259.
[9] Fuoss, *J. Amer. Chem. Soc.*, 1935, **57**, 488.
[10] Åkerlöf, *ibid.*, 1932, **54**, 4132.
[11] S. C. R. Hughes, *J.*, 1956, 998.

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Owen and Waters [12] obtained $K = 2{\cdot}0 \times 10^{-4}$ for the dissociation of hydrochloric acid in 18% (w/w) water in dioxan ($D = 9{\cdot}53$ at 25°). This constant is nearly the same as ours in 3%

TABLE 1. *Effect of the initial concentration of* $Ph_3C{\cdot}Cl$ *on the rate of hydrolysis.*

	10^3k (sec.$^{-1}$)		
$[Ph_3C{\cdot}Cl]_0$	1·35M-H_2O	1·67M-H_2O	2·46M-H_2O
0·026	4·35	7·2	21·0
0·050	4·75	7·7	20·5
0·079	5·00	—	20·2
0·10	5·3	—	20·0

TABLE 2. *Rate constants (sec.$^{-1}$) of the forward reaction and activation energies (E_a, kcal./mole) in the hydrolysis of 0·05M-triphenylmethyl chloride in aqueous acetone.*

$[H_2O]$ (M)		0·55	$0{\cdot}93_5$	1·35	1·67	2·31	2·64	2·98	3·88
H_2O (% v/v)		1·00	1·68	2·44	3·01	4·15	4·76	5·36	6·98
10^3k	29·5°	2·00	2·90	4·75	7·67	17·3	25·0	36·2	
	14·4°	$0{\cdot}61_5$	1·00	1·72	2·50	5·50	8·35	11·9	25·5
	0·0°	$0{\cdot}14_3$	$0{\cdot}23_4$	0·42	$0{\cdot}66_5$	1·47	2·17	3·42	8·16
E_a		15·0	14·3	13·6	13·8	14·0	13·7	13·0	12·6

TABLE 3. *Fraction of triphenylmethyl chloride hydrolysed at equilibrium.*

Initial concentration = 0·05M.

$[H_2O]$ (M)		0·55	$0{\cdot}93_5$	1·36	1·67
H_2O (% v/v)		1·00	1·68	2·44	3·06
Reaction (%)	29·5°	75	85	92·5	100
	14·4°	81	93·5	100	
	0·0°	85	100		

TABLE 4. *Effect of lithium chloride and perchlorate, silver nitrate, perchloric acid, hydrochloric acid, and phenol on the rate constants (sec.$^{-1}$) at 29·5°.*

$[RCl]_0 = 0{\cdot}05$M, $[H_2O] = 1{\cdot}67$M (3% v/v) unless otherwise indicated. All concentrations mM.

[LiCl]	$[Cl^-]$ *	10^3k	$[LiClO_4]$	10^3k	$[HClO_4]$	10^3k	[Ph·OH]	$[H_2O]$	10^3k
0	2·40	7·67	0	7·67	0	7·67	0	830	2·5
6	2·84	6·41	3	9·85	2·5	9·35		1350	4·75
12	4·00	5·67	6	10·0	[HCl]	10^3k		1670	7·67
18	4·91	5·25	$[AgNO_3]$ †	10^3k	0	7·67	10	830	2·5
24	5·6	4·84	0	2·0	12	8·25		1350	4·75
			50	2·33	24	8·75		1670	7·67

* Mean free chloride-ion concns. calc. from dissociation constants.
† $[H_2O] = 0{\cdot}55$M (1% v/v).

water in acetone and their equivalent conductance plot resembles ours closely. Results are given in Tables 1—4. The rate constants at 29·5° in 1·35M-H_2O and 1·35M-D_2O (isotopic enrichment 95%) are 4·75 and $3{\cdot}66 \times 10^{-3}$ sec.$^{-1}$ so $k_{D_2O}/k_{H_2O} = 0{\cdot}77$.

DISCUSSION

Reaction Order.—The kinetics in aqueous acetone follow the first-order rate equation (eqn. 5) strictly. The rate constants depend to some extent on the initial concentration of the alkyl halide, especially at very low water contents (Table 1) where probably some bimolecular substitution also occurs. No definite dependence of order on water concentration can be established. Such a dependence would require a linear plot of log k–log $[H_2O]$ with a slope equal to n, the order with regard to water: $-d[RCl]/dt = k[RCl][H_2O]^n$. Even at 1% water in acetone, the water concentration exceeded ten times the alkyl halide concentration and can be assumed not to change effectively during a run: $-d[RCl]/dt = k'[RCl]$, where $k' = k[H_2O]^n$ and hence $\log k' = n \log [H_2O] + \text{const.}$ Fig. 2 displays a parabola with no distinct linear parts. Consequently the " push-pull " mechanism proposed by Swain,[13] according to which two water molecules participate actively (*i.e.*,

[12] Owen and Waters, *J. Amer. Chem. Soc.*, 1938, **60**, 2371.
[13] Swain, *J. Amer. Chem. Soc.*, 1948, **70**, 1124.

changing their covalent bonds and thereby contributing to the order of reaction) in the transition state, does not fit this hydrolysis in aqueous acetone.

Effect of the Water Content in Acetone on the Rate of Hydrolysis.—The observed rate constants depend markedly on the water content in acetone (Table 2; Fig. 3). This must be related to the ionizing power of the solvent. The rate-determining step is the heterolysis of the carbon–halogen bond: $RCl \longrightarrow R^+ + Cl^-$. In the gaseous phase the energy required for this fission equals the heat of ionization. In solution this energy is lowered considerably owing to the heat of solvation of the produced ions. The solvation of the ions is achieved mainly by water molecules and this process is easier the higher the water content in acetone. Therefore a rise in the rate constants and a decrease in activation energy with increased water content is observed.

In fact, E_a in Table 2 does not represent true activation energies, because they were calculated by means of the Arrhenius equation from the *observed* rate constants. As will be shown, these observed rate constants are composed of rate constants of several reactions,

FIG. 2. *Effect of water on the hydrolysis rate.*

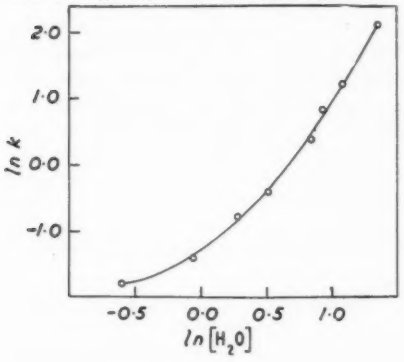
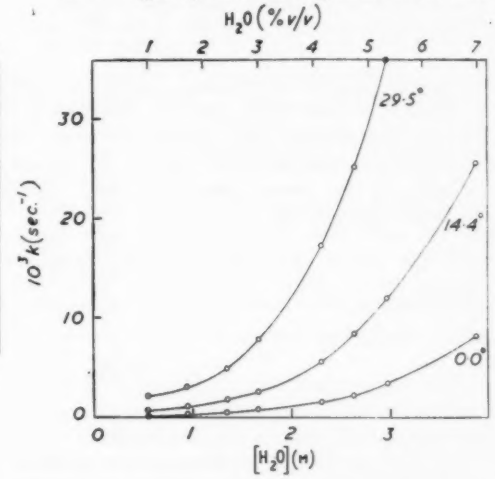


FIG. 3. *Effect of water and temperature on the rate.*



each of which is affected differently by varying the acetone–water ratio. Thus the term " temperature coefficient " would be more appropriate than activation energy.

Mass-law and Ionic-strength Effects.—The linearities of the kinetic plots appear at first sight to contradict the S_N1 scheme and its consequences. According to this scheme, deviation from first-order kinetics during a run is expected owing to the mass-law effect. Although the ionic-strength effect tends to neutralize it, in general they do not counteract one another exactly. Moreover, the addition of lithium chloride, a common-ion salt, causes a very significant decrease of the observed rate constant (Table 4) although it increases the ionic strength. Further, one cannot expect a small value for α, the mass-law constant, since even less stable ions have a value of tens for this constant.[1] This is clarified by consideration of the small dissociation of hydrochloric acid in acetone of low water content. The absolute increase of the free chloride-ion concentration during a run is so small that neither a marked mass-law effect nor an ionic-strength effect can be detected.

Table 5 gives the kinetics when the water content is the mean of the range investigated. The concentrations of the hydrochloric acid liberated in the hydrolysis are given in the third column. About half the triphenylmethyl chloride was already decomposed when measurements started owing to its decomposition in the stock solution and to the reaction which occurs before the first reading can be taken.

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In the fourth column of Table 5 the free chloride-ion concentrations are listed, calculated from the dissociation constant. d_1 is the value of the denominator of eqn. (4), α^0 being taken as 6×10^3 (the estimation of the mass-law constant is given below). We applied the reduced eqn. (4) because the antilogarithmic factors of eqn. (3) containing the ionic strength in the first power do not differ much from unity. In 3% water in acetone,[10] D is 20 at 302·7°K, and taking the mean ionic strength $= 2{\cdot}4 \times 10^{-4}$, one obtains antilog $(-CI) = 0{\cdot}99$. The ionic-strength constants, σ, estimated by Hughes, Ingold, and co-workers for various alkyl halides are $1—3 \times 10^{-8}$. Assuming for triphenylmethyl chloride a mean value of 2×10^{-8}, we get antilog $(B\sigma I) = 0{\cdot}97$.

TABLE 5. *Detailed kinetics of the hydrolysis of* 0·05M-*triphenylmethyl chloride in* 1·67M-*water* (3% *v/v*) *in acetone at* 29·5°

Time (min.)	$\log \frac{c_\infty - c_0}{c_\infty - c_t}$	10^3[HCl] (M)	10^3[Cl⁻] (M)	d_1	d_2	Time (min.)	$\log \frac{c_\infty - c_0}{c_\infty - c_t}$	10^3[HCl] (M)	10^3[Cl⁻] (M)	d_1	d_2
0·00	0·00	26·6	2·16	6·70	2780	1·01	0·46	33·8	2·44	7·15	5100
0·18	$0{\cdot}08_5$	28·2	2·24	6·85	3220	1·46	0·67	36·0	2·52	7·25	5950
0·40	0·18	29·9	2·30	6·95	3750	2·12	$0{\cdot}96_4$	38·5	2·60	7·38	7150
0·67	0·31	31·7	2·36	7·04	4250	2·57	1·17	39·9	2·66	7·45	7930

$k = 7{\cdot}67 \times 10^{-3}$ sec.$^{-1}$; $t_{\frac{1}{2}} = 1{\cdot}5$ min.

The denominator (d_1) varies by *ca.* 5% about the mean value during the measurements. It should be noted that the free chloride-ion concentrations are calculated from the dissociation constant of HCl which is valid only in very dilute solutions. At the centimolar concentrations applied in the kinetics, the accumulation of the ions and consequently the deviation of the denominator from the mean during a run are probably even smaller. Therefore one may write:

$$\frac{k_1^0}{\alpha^0\,[\mathrm{Cl}^-]\,\text{antilog}\,(AI^{\frac{1}{2}}) + 1} \simeq \text{const.} = k \qquad . \quad . \quad . \quad . \quad . \quad (6)$$

where k is the observed forward rate constant. Introducing eqn. (6) into (5) we get:

$$kt = \frac{k_1^0 t}{\alpha^0[\mathrm{Cl}^-]\,\text{antilog}\,(AI^{\frac{1}{2}}) + 1} = \log \frac{c_\infty - c_0}{c_\infty - c_t} \qquad . \quad . \quad . \quad . \quad (7)$$

Thus the linearity of the kinetic plots is understandable. The observed rate constants obtained from the slopes of the plots have a very complex meaning.

For comparison, the fifth column of Table 5 (d_2) lists the values of the denominator of eqn. (3) by assuming that all the hydrochloric acid dissociates into ions. In this hypothetical case the deviation from the mean is immense and obviously the kinetic plots would not be linear.

The mass-law constant is estimated from the rate constants in presence of lithium chloride. The estimate is approximate, because we do not know exactly the chloride-ion concentration in the presence of one salt, let alone in a mixture of lithium chloride and hydrochloric acid. Assuming, however, that only the former contributes the ions (its dissociation constant is 8 times that of the acid) and that the dissociation constant calculated for infinite dilution is valid also for the concentrations used, and disregarding the antilogarithmic factors containing the ionic strength in the first power, one obtains, according to eqn. (6),

$$\frac{k_a}{k_b} = \frac{\alpha^0[\mathrm{Cl}^-]_b\,\text{antilog}\,(AI_b^{\frac{1}{2}}) + 1}{\alpha^0[\mathrm{Cl}^-]_a\,\text{antilog}\,(AI_a^{\frac{1}{2}}) + 1} \qquad . \quad . \quad . \quad . \quad . \quad (8)$$

where k_a and k_b are the observed rate constants in presence of chloride-ion concentrations $[\mathrm{Cl}^-]_a$ and $[\mathrm{Cl}^-]_b$ respectively. If pairs of the ion concentrations and rate constants listed in Table 4 are introduced successively in eqn. (8), the following average is obtained for the mass-law constant: $\alpha^0 = (6 \pm 3) \times 10^3$. The accuracy is very low, which is not surprising in view of the many approximations.

The above mass-law constant relates to 97% acetone. In other acetone–water mixtures different constants are to be expected, because the specific rates, k_2^0 and k_3^0, constituting α^0, are not affected to the same degree by the change of the medium. For instance, Bensley and Kohnstam [14] found that the mass-law constant for dichlorodiphenylmethane in 85% acetone is 126 and in 75% acetone 79. (On the effect of the medium on rate constants, see following paper.)

Using the above value of α^0, one may obtain for the rate of dissociation of triphenylmethyl chloride in 97% acetone at 29·5°:

$$k_1^0 = k\,\alpha^0\,[Cl^-]\,\text{antilog}\,(AI^{\frac{1}{2}}) + k = 5{\cdot}5 \times 10^{-2}\,\text{sec.}^{-1}$$

where $k = 0{\cdot}00767$ sec.$^{-1}$ (observed rate constant) and $[Cl^-] = I = 0{\cdot}0024$ (the mean free chloride concentration during a run).

Thus the rate of dissociation at zero ionic strength of such a rapid reaction can be calculated. The measurement of this rate by ordinary means seems almost impossible.

Effect of Additives on the Rate of Hydrolysis.—Lithium perchlorate increases notably the observed rate constant (Table 4), in accordance with the ionic-strength effect. The ionic strength decreases the rate of the reassociation of the ions and consequently the overall rate of hydrolysis increases.

Added silver nitrate accelerates the reaction (Table 4). Almost no reassociation occurs and the observed rate should nearly equal the rate of the dissociation of triphenylmethyl chloride. But since a precipitate is formed, the medium is not homogeneous and no quantitative conclusions should be drawn. Indeed, no linear kinetic plot is obtained in this case: the slope increases toward the end of the reaction.

Perchloric acid (Table 4) increases the rate noticeably, in conformity with the ionic-strength effect. Here some hydrogen bonding between the leaving halogen atom and the perchloric acid may play some rôle. Furthermore, because of the high degree of dissociation of this acid, a depression of the dissociation of the hydrochloric acid is to be expected and this also decelerates the reassociation.

Hydrochloric acid has little effect, only slightly accelerating the hydrolysis. It is, in any case, liberated during reaction.

Of special interest is the effect of a non-ionic additive on the rate of hydrolysis. In its presence the solvation process may be affected. Phenol is generally employed as a " solvation agent " in unimolecular reactions. Hudson and Saville [7] noted an acceleration of the alcoholysis of triphenylmethyl chloride in carbon tetrachloride in the presence of phenol and similar results were obtained by Swain and Kreevoy [15] in the radiochloride exchange of triphenylmethyl chloride in benzene. The rate of hydrolysis of this chloride in aqueous acetone is not changed by the presence of phenol (Table 4). Probably phenol is an excellent solvating agent compared with carbon tetrachloride and benzene, but it is a poor competitor compared with water or acetone.

The rate of hydrolysis in presence of heavy water also indicates the importance of the solvation, the rate being markedly depressed. It is well known that hydrogen bonds between the leaving halide ion and deuterium are weak compared with those with ordinary hydrogen.[16,17,18] The rates of hydrolysis of typical unimolecular reactions in heavy water are usually only 0·7—0·8 of those in ordinary water, as is observed here. The rates of bimolecular reactions are generally not affected by interchanging the two kinds of water.[18]

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[14] Bensley and Kohnstam, *J.*, 1955, 3408.
[15] Swain and Kreevoy, *J. Amer. Chem. Soc.*, 1955, **77**, 1122.
[16] Streitwieser, *Chem. Reviews*, 1956, **56**, 655.
[17] Olivier, *Rec. Trav. chim.*, 1937, **56**, 247.
[18] Swain, Cardinaud, and Ketley, *J. Amer. Chem. Soc.*, 1955, **77**, 934.

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265. *The Second (Rapid) Step in the Nucleophilic Substitution of Alkyl Halides. Part II.* Competitive Substitution Reactions.*

By D. Golomb.

The course of competitive substitution reactions of some alkyl halides is outlined, in which an ionic substituent (azide or thiocyanate) competes with a molecular one (water) for the same carbonium ion (triphenylmethyl, diphenylmethyl, di-*p*-tolylmethyl) yielding the alkyl azide or thiocyanate and the alcohol, which are all stable. The combination of the solvents and presence of various additives affect differently the activities of the reacting species and, in particular, that of the carbonium ion and ionic substituent. This is established by analysis. Decrease in dielectric constant usually increases the ratio of alkyl azide (thiocyanate) to alcohol; increase of ionic strength decreases it.

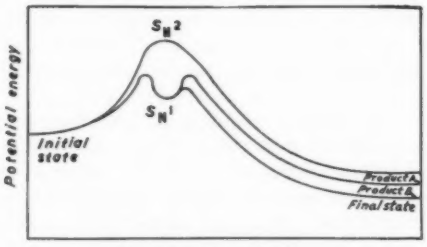
For the hydrolysis of triphenylmethyl chloride, a scheme was adopted * according to which two substituting agents—one molecular and one ionic—compete for the carbonium ion, but only one product is obtained—the alcohol; the other reaction is the reassociation between the carbonium and the halide ion. Yet the kinetic process is complicated by this competition to an extent indicated by $\alpha = k_2/k_3$, the ratio of the rates of the competing reactions.

If we add some other ionic substituent to the reaction mixture, say azide ions, three substituents (halide, azide, and water) compete for the carbonium ion, yielding the corresponding alcohol and alkyl azide, which are both stable:[1,2]

$$RX \underset{k_3}{\overset{k_1}{\rightleftharpoons}} R^+ + X^-; \quad R^+ + N_3^- \xrightarrow{k_2'} RN_3; \quad R^+ + H_2O \xrightarrow{k_2} ROH . \quad (1)$$

Because of the similarity of the reassociation and the carbonium ion–azide reaction, information on the mechanism is available from the product-ratio in various media and in the presence of added materials.

As in the previous paper, we assume that the carbonium ion produced as an intermediate lasts sufficiently long to be treated as a separate electrochemical entity, *i.e.*, possessing an ionic radius, solvation layer, ionic atmosphere, activity, etc. Accordingly the life of the carbonium ion must exceed 10^{-8}—10^{-10} sec., the time of building up of an ionic atmosphere.[3]



The potential energy curve of a competitive substitution is illustrated in the Figure. The lower curve represents the energetics of a unimolecular competitive substitution. After acquiring sufficient activation, the alkyl halide decomposes into the ions. The

* Part I, preceding paper.

[1] Bateman, Hughes, and Ingold, *J. Amer. Chem. Soc.*, 1938, **60**, 3080.
[2] *Idem, J.*, 1940, 974.
[3] Harned and Owens, "Electrolytic Solutions," Reinhold Publ. Co., New York, 1950; Chap. IV.

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solvation of the ions lowers their potential energy as shown by the valley which may be considered as an initial state of two reactions; each one in order to reach completion must pass an energy hill of different height. For comparison, the energetics of a bimolecular substitution is given by the upper curve. In a bimolecular competitive substitution two such curves must be drawn, which would differ along their entire lengths.

Hughes, Ingold, *et al.*[2,4] made a hypothesis that the carbonium ion–water reaction requires no activation because it occurs between the carbonium ion and one of the water molecules of the hydration shell surrounding the ion, simply by " collapse " of the shell. Thus if the water content exceeds the minimum necessary to build up a hydration shell, the water in the bulk of the solution no longer affects the rate of the carbonium–water reaction.

Our results do not support the " collapse " hypothesis. The relative amounts of products of competitive substitution of triphenyl- and diphenyl-methyl chloride are largely dependent on the water content of the solvent. The substitution products of di-*p*-tolyl-methyl chloride are less sensitive to the solvent composition, but even there a trend is noticeable. Therefore we believe that the carbonium ion may react with any water molecule from the solution and not only with one of the hydration shell. Probably the particular molecule has to be activated in order to react.

The rates of reaction of the carbonium ion with an ion (k_2') and a molecule (dipole) (k_3) are differently affected by the ionic-strength:

$$\log k_2 = \log k_2^0 + AI^{\frac{1}{2}} * \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$\log k_3 = \log k_3^0 + CI \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where A and C have the same meanings as in the preceding paper, and the index zero denotes zero ionic strength. The rate ratio of the two competing reactions at ionic strength I is:

$$k_2/k_3 = (k_2/k_3)_0 \text{ antilog } (AI^{\frac{1}{2}} - CI) \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Since A is negative, it is evident from eqn. (4) that this ratio decreases with increasing ionic strength.

In the case of a non-competitive hydrolysis of an alkyl halide, the ionic-strength effect slows the reassociation and thereby increases the overall hydrolysis rate. In a competitive substitution, the increasing ionic strength slows the carbonium ion–ion reaction (and also the reassociation) and thereby increases the share of alcohol in the products.

The rates of the two competing reactions are not sensitive in the same manner to the dielectric constant, D, whose effect on an ion–ion interaction is calculated by Scatchard.[5]

$$\log (k_2)_D = \log (k_2)_\infty - \frac{z_A z_B e^2 N}{2{\cdot}3\, DRT r_2^\ddagger} \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

where $r_2^\ddagger$ is the distance between the ions in the transition state, $(k_2)_D$ and $(k_2)_\infty$ are the rates at D and infinite dielectric constant respectively; z_A and z_B denote the charges of the ions. In the carbonium-ion–ion reaction $z_A z_B = -1$. Laidler and Eyring [6] calculated the effect of the dielectric constant on an ion–dipole interaction:

$$\log (k_3)_D = \log (k_3)_\infty + \frac{z^2 e^2 N}{2 \times 2{\cdot}3 DRT} \left(\frac{1}{r} - \frac{1}{r_3^\ddagger} \right) \quad . \quad . \quad . \quad . \quad (6)$$

* One should write k_2' and $k_3'^0$, but the prime will be omitted for convenience and because of the similarity to the reassociation.

[4] Hawdon, Hughes, and Ingold, *J.*, 1952, 2499.
[5] Scatchard, *J. Amer. Chem. Soc.*, 1930, **52**, 52.
[6] Laidler and Eyring, *Ann. N.Y. Acad. Sci.*, 1940, **39**, 303.

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where r is the radius of the ion, $r_3^{\ddagger}$ is the distance between the ion and the centre of the dipole axis in the transition state.

Combination of eqns. (5) and (6) gives:

$$\left(\frac{k_2}{k_3}\right)_D = \left(\frac{k_2}{k_3}\right)_\infty \text{antilog}\left\{\frac{Ne^2}{2{\cdot}3DRT}\left(\frac{1}{r_2^{\ddagger}} - \frac{1}{2r} + \frac{1}{2r_3^{\ddagger}}\right)\right\} \quad . \quad . \quad . \quad (7)$$

According to equation (7), the rate ratio of the two competing reactions decreases with increasing dielectric constant. In the non-competitive hydrolysis of an alkyl halide, the increasing dielectric constant brings about a deceleration of the reassociation reaction (*i.e.*, α decreases), whereas in a competitive substitution it causes an increase of the rate of the carbonium ion–dipole reaction and consequently the proportion of alcohol in the products becomes higher.

It is difficult to exploit eqns. (4) and (7) quantitatively. Eqn. (4) is valid only at infinite dilutions and eqn. (7) requires the knowledge of interionic and ion–dipole distances which are so far very obscure. Usually plots of rates against the reciprocal of the dielectric constant are drawn to determine, by extrapolation to infinite dielectric constant, the factors containing the radii in eqn. (5) or (6).[7] Equation (7) applies to competitive substitution, which is more complicated because we deal with ratios of unmeasurably fast rates. Further, Scatchard's and Laidler and Eyring's equations treat a salt solution as a continuous dielectric which is not true for real concentrations.[8]

These restrictions being considered, eqns. (4) and (7) only help toward a better qualitative understanding of the course of competitive substitution reactions of alkyl halides in various media in the presence of salts.

Experimental

Materials.—Di-*p*-tolylmethyl chloride, obtained by passing dry hydrogen chloride through an ethereal solution of the alcohol (prepared by reduction of commercial *pp'*-dimethylbenzophenone with lithium aluminium hydride) over calcium chloride,[2] had m. p. 43°. Diphenylmethyl chloride was prepared similarly. Dioxan was purified according to Beste and Hammett [9] by successive refluxing over sodium hydroxide and sodium. Sodium azide was recrystallized from aqueous alcohol.[10] Diphenylguanidine was recrystallized from aqueous acetone. For the preparation of triphenylmethyl chloride and acetone, see preceding paper.

Analysis of Products.—In the solvents used, all the alkyl halides react completely, yielding the alcohol and the alkyl azide or alkyl thiocyanate. Hydrochloric acid is developed in equivalent amounts to the alcohol. Thus the product ratio is calculated by:

$$[\text{ROH}]/[\text{RN}_3] = x/(a - x) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

where x is the titre of the acid liberated in the competitive substitution and a is the acid liberated by complete hydrolysis of the alkyl halide (*i.e.*, without addition of sodium azide or thiocyanate).

Hydrochloric acid in the presence of such a weak salt as NaN_3 or NaSCN behaves like a buffer and consequently no sharp change of colour is observed by titration with indicators. However, conductometric titration of the acid with a weak base gives very good results [11] even in the presence of highly conducting salts like $LiClO_4$ and $LiNO_3$. The weak base used as a titrant was 0·1N-diphenylguanidine [12] ($pK = 10$) in 75% acetone–25% water. Conductances were measured with the apparatus in the preceding paper.

The alkyl halide, in acetone or dioxan, was brought to thermostat temperature. Aqueous sodium azide or thiocyanate with or without other salts added was introduced quickly with a syringe pipette into the well-stirred solution. After about ten half-times of reaction, the solution was diluted with 75% acetone to make up 100 ml. and the acid was titrated as above.

[7] Amis and LaMer, *J. Amer. Chem. Soc.*, 1939, **61**, 905.
[8] Hasted, Ritson, and Collie, *J. Chem. Phys.*, 1948, **16**, 1.
[9] Beste and Hammett, *J. Amer. Chem. Soc.*, 1940, **62**, 2481.
[10] *Inorg. Synth.*, 1939, **1**, 80.
[11] Grunwald, Florida State Univ., Tallahassee, Fla., personal communication.
[12] Hall and Sprinkle, *J. Amer. Chem. Soc.*, 1932, **54**, 3469.

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Aqueous dioxan reaction mixtures were also diluted with aqueous acetone to yield better conductometric plots.

The alkyl thiocyanates are not very stable. Swain *et al.*[13] reported that triphenylmethyl thiocyanate decomposes in 75% acetone at 25° with $k = 7 \times 10^{-4}$ sec.$^{-1}$, so the corresponding half-time is about 17 min., which is rather short. Therefore sodium thiocyanate was used as a substituent, as follows. After 4—5 half-times of reaction of the corresponding alkyl halide, the solution was quenched with ice-cold aqueous acetone and titrated quickly. The alkyl chlorides react much faster than the thiocyanates, so only minute amounts of the latter decompose during the process. Nevertheless, the results with thiocyanate are not as accurate as those with azide. Rate constants of the decomposition of the diphenylmethyl chlorides were determined by Hughes, Ingold, and co-workers[2,14] and of triphenylmethyl chloride by us (preceding paper). Results are in Tables 1 and 2.

TABLE 1. *The percentage of alkyl azide in the products upon completed competitive substitution of* 0·05M-RCl *in aqueous acetone and aqueous dioxan at* 25°.

Row *a*: in presence of 0·05M-NaN_3; *b*: in presence of 0·05M-NaN_3 and 0·25M-$LiClO_4$; *c*: in presence of 0·05M-NaN_3 and 0·25M-$LiNO_3$. Di = dioxan, Ac = acetone.

Solvent		Di 87·5%	Di 75%	Ac 87·5%	Ac 75%	Ac 66·7%	Ac 50%
D		7·5	14	25	31·5	36·5	47
$Ph_2C{\cdot}Cl$	*a*	89·7	82·5	62	50	33	—
	b	86·7	59	57	30·5	12	—
	c	88	68·5	58·5	36·5	23·5	—
	a/*b*	1·03	1·40	1·09	1·64	2·75	—
	a/*c*	1·02	1·20	1·08	1·37	1·40	—
$(CH_3{\cdot}C_6H_4)_2CH{\cdot}Cl$	*a*	58	51	59	56·3	54·5	50
	b	44·5	40	50·7	47·5	44	—
	c	45	39	51·5	47·5	43·5	—
	a/*b*	1·30	1·27	1·16	1·18	1·24	—
	a/*c*	1·29	1·31	1·15	1·18	1·25	—
$Ph_2CH{\cdot}Cl$	*a*	—	22	24	15·5	12	—
	b	—	11	20·5	9·5	—	—
	c	—	12·5	19	9·5	—	—
	a/*b*	—	2·00	1·17	1·63	—	—
	a/*c*	—	1·76	1·26	1·63	—	—

TABLE 2. *The percentage of alkyl thiocyanate in the products.*

Conditions as stated in Table 1, except that NaSCN is present instead of NaN_3.

Solvent		Di 75%	Ac 87·5%	Ac 75%	Ac 66·7%
D		14	25	31·5	36·5
$Ph_2C{\cdot}Cl$	*a*	—	55	34·5	24·5
	b	—	51	32	21
	c	—	49·5	30·5	23·3
	a/*b*	—	1·08	1·08	1·17
	a/*c*	—	1·11	1·13	1·05
$Ph_2CH{\cdot}Cl$	*a*	31·5	—	—	—
	b	29	—	—	—
	c	29	—	—	—
	a/*b*	1·09	—	—	—
	a/*c*	1·09	—	—	—

DISCUSSION

Effect of Dielectric Constant on Competitive Substitution.—According to eqn. (7), increase of the dielectric constant should decrease k_2/k_3 and yield a lower proportion of the alkyl azide. Table 1, row *a*, shows that triphenylmethyl chloride obeys this rule even when passing from one organic solvent to the other, whereas the diphenylmethyl chlorides obey it only within the same solvent. This may be due to the variation of the factor containing

[13] Swain, Scott, and Lohmann, *J. Amer. Chem. Soc.*, 1953, **75**, 136.
[14] Hughes, Ingold, and Taher, *J.*, 1940, 949.

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the radii when passing from one solvent to the other. The decrease of the amount of ditolylmethyl azide in the products with decreasing water content in acetone is well distinguishable, in contrast to the statement of Bateman, Hughes, and Ingold [2] (cf. p. 1335) relating to the "collapse" hypothesis. These authors analyzed the products by titrating the liberated acid with the aid of an indicator, but this method is rather insensitive for detection of the variations of the product ratio.

Effect of Ionic Strength on Competitive Substitution.—According to eqn. (4), an increase of ionic strength should decrease k_2/k_3 and yield a lower proportion of alkyl azide. This is confirmed in all experiments (Tables 1 and 2, rows *b* and *c*). The ionic strength was increased by addition of inert salts (lithium perchlorate and nitrate) in concentrations exceeding five-fold that of the reactants. These salts do not yield stable products with the alkyl halides used in aqueous solutions.[15] If alkyl perchlorates or nitrates were formed as intermediates during reaction, they would decompose rapidly to reproduce the same carbonium ion.

The constants A and C of eqn. (4) contain the dielectric constant in the denominator. Accordingly one would expect the effect of ionic strength to decrease with increasing water content in the solvent. Rows *a*/*b* and *a*/*c* indicate, however, that the contrary is true. Presumably this is to be attributed to the increasing degree of dissociation of the salts in solvents of higher water contents which causes a rise in the ionic strength. The fact that $LiClO_4$ usually produces a larger effect than $LiNO_3$ is probably also due to the higher degree of dissociation of the former (ref. 3, p. 564).

For this and the preceding paper I thank Professor I. Dostrovsky for guidance; Professor E. Grunwald, Dr. A. Oplatka, and members of the Isotope Department for discussions, and Dr. M. Cohen for reading the manuscripts.

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[15] Hofmann and Kirmreuther, *Ber.*, 1909, **42**, 4861.

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266. *Polymerisation of Epoxides. Part I. Some Kinetic Aspects of the Addition of Alcohols to Epoxides catalysed by Sodium Alkoxides.*

By Geoffrey Gee, W. C. E. Higginson, (Miss) P. Levesley, and K. J. Taylor.

The kinetics of the base-catalysed addition of alcohols to ethylene oxide have been studied. These reactions are of first order in ethylene oxide. Apparent orders of less than unity in the catalyst (sodium alkoxide) concentration are ascribed to incomplete dissociation, the ion-pair being much less reactive than the free alkoxide ion. In most cases the rate depends upon the concentration of alcohol, but this is ascribed to the effect of the latter on the degree of dissociation of the sodium alkoxide. There is no evidence to suggest that the reaction is termolecular, *i.e.*, that it involves the necessary presence of an alcohol molecule in the transition complex.

Apparent rate constants are given for the addition of various alcohols to ethylene oxide, the pure alcohol acting as the solvent. True rate constants have been measured for the addition of methanol to several epoxides in solution in pure methanol, and reveal a marked retardation by alkyl substitution.

Although there have been many kinetic studies of addition reactions involving olefin oxides,[1] the addition of alcohols catalysed by the corresponding alkoxide ions has not been investigated in detail. Boyd and Marle [2] studied the addition to olefin oxides of

[1] See Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, pp. 341—344.

[2] Boyd and Marle, *J.*, 1914, **105**, 2117.

phenols catalysed by their sodium salts, and concluded that reaction occurs between the phenoxide ion and the olefin oxide. By analogy with this reaction the addition of an alcohol is likely to involve the reactions

$$RO^- + C_2H_4O \longrightarrow RO{\cdot}CH_2{\cdot}CH_2{\cdot}O^-$$

$$RO{\cdot}CH_2{\cdot}CH_2{\cdot}O^- + ROH \rightleftharpoons RO{\cdot}CH_2{\cdot}CH_2{\cdot}OH + RO^-$$

Apart from its intrinsic interest, this class of reaction is of importance in its relation to the base-catalysed polymerisation of olefin oxides,[3] which is thought to proceed through the following steps:

$$B^- + C_2H_4O \longrightarrow B{\cdot}CH_2{\cdot}CH_2{\cdot}O^- \rightleftharpoons B{\cdot}CH_2{\cdot}CH_2{\cdot}OH$$

$$B{\cdot}CH_2{\cdot}CH_2{\cdot}O^- + C_2H_4O \longrightarrow B(CH_2{\cdot}CH_2{\cdot}O)_2^- \rightleftharpoons B(CH_2{\cdot}CH_2{\cdot}O)_2H$$

$$B(CH_2{\cdot}CH_2{\cdot}O)_n^- + C_2H_4O \longrightarrow B(CH_2{\cdot}CH_2{\cdot}O)_{n+1}^- \rightleftharpoons B(CH_2{\cdot}CH_2{\cdot}O)_{n+1}H$$

Except for the initial reaction, all the steps are of the above type, and the initial reaction is also similar when B^- is an alkoxide ion. In a system giving low-molecular-weight polymers, the rates of the successive steps, other than the first, are [4] closely similar, but no detailed kinetic study has been made.

In the addition of amines to ethylene oxide in aqueous solutions, Eastham [5] concludes that the water plays an important part, while in pyridine solution a proton-source (the pyridinium ion) is essential. Thus the rate of addition of an alcohol to an olefin oxide may depend on the alcohol concentration as well as on that of the olefin oxide and the catalyst. In the first section of this paper we report a kinetic investigation of the addition of various alcohols to ethylene oxide, catalysed by the corresponding alkoxide ions. The overall reaction, if excess of alcohol is present, is $ROH + C_2H_4O \longrightarrow RO{\cdot}C_2H_4{\cdot}OH$ and is accompanied by a decrease in volume, making possible the use of dilatometry. This method was shown to be satisfactory by parallel experiments in which the concentration of ethylene oxide was determined analytically. In preliminary experiments the rates of reaction of ethylene oxide with various alcohols were found, the pure alcohol being the solvent. The initial concentrations of ethylene oxide were 1—2M, alcohol being in at least five-fold excess. Under these conditions good first-order plots were obtained up to 90% consumption of ethylene oxide, and Table 1 shows the first-order velocity constants $k_1 = -\mathrm{d} \ln [C_2H_4O]/\mathrm{d}t$ and the corresponding concentrations of the sodium alkoxide catalyst. Except where stated, in these and subsequent experiments the temperature was 29·8°. In similar experiments with *tert.*-butyl alcohol and *cyclo*hexanol the value of k_1 was found to increase with the extent of reaction.

TABLE 1.

[Alcohol] (M)	10[NaOR] (M)	10^5k_1 (sec.$^{-1}$)	10^5k_2 (l. mole^{-1} sec.$^{-1}$)	[Alcohol] (M)	10[NaOR] (M)	10^5k_1 (M)	10^5k_2 (l. mole^{-1} sec.$^{-1}$)
$CH_3{\cdot}OH$	2·63	5·63	21·4	$CH_3{\cdot}O{\cdot}C_2H_4{\cdot}OH$ ...	3·54	6·62	18·7
$C_2H_5{\cdot}OH$	0·68	3·74	55·0	$C_2H_5{\cdot}O{\cdot}C_2H_4{\cdot}OH$ ...	1·17	1·77	15·1
n-$C_3H_7{\cdot}OH$	1·25	7·30	58·5	$CH_3{\cdot}[O{\cdot}C_2H_4]_2{\cdot}OH$...	2·67	3·15	11·8
n-$C_4H_9{\cdot}OH$	0·97	4·57	47·1	$C_2H_5{\cdot}[O{\cdot}C_2H_4]_2{\cdot}OH$	2·72	4·51	16·6
$HO{\cdot}[CH_2]_2{\cdot}OH$ ...	1·76	3·71	21·1	$C_2H_5{\cdot}[OC_2H_4]_3{\cdot}OH$...	2·09	2·36	11·3
$HO{\cdot}[CH_2]_3{\cdot}OH$ ...	0·62	3·94	63·6				

The variation of k_1 with the concentration of the catalyst was investigated for certain alcohols, and some of the results are shown in Fig. 1. In the methanol–sodium methoxide system the reaction is strictly of first order in sodium methoxide, but in all the other cases the order in catalyst is slightly less than unity, as can be seen from the curvature of the plots. Other experiments were performed to find the effect of the concentration of the alcohol upon the rate, 1 : 4-dioxan being used as an inert diluent. In a series of

[3] Perry and Hibbert, *J. Amer. Chem. Soc.*, 1940, **62**, 2599.
[4] Miller, Bann, and Thrower, *J.*, 1950, 3623.
[5] Eastham, *ibid.*, 1952, 1936.

experiments in which the alcohol concentration was varied, comparison was made through a second-order constant, $k_2 = k_1/[\mathrm{NaOR}]$, as shown in Table 1. For a given alcohol, variations in the catalyst concentration were not large, so that the errors introduced on account of the non-integral order in the catalyst were small. Fig. 2 shows plots of k_2' against x for various alcohols, where x is the ratio of the concentration of alcohol (in mole $l.^{-1}$) to its concentration when the pure alcohol is used as solvent, and k_2' is the ratio of k_2 at alcohol concentration x to k_2 when $x = 1$. The plots are similar for ethanol, propan-1-ol, butan-1-ol, and 2-ethoxyethanol, but these differ considerably from methanol, while the behaviour with glycol is intermediate between these extremes. Since the dielectric constant of the solvent is reduced when the concentration of alcohol is decreased, at least two effects may be responsible for the changes in k_2 with x. Hence, several sets of experiments were done in which the alcohol concentration was varied, the dielectric constant being maintained at approximately the same value for experiments in a given set by the use of 1 : 4-dioxan ($D \simeq 2$) and nitrobenzene ($D \simeq 34$);* some results are shown

FIG. 1. *Reactions in: a propan-1-ol, b butan-1-ol, c methanol, and d 70% butanol–30% dioxan.*

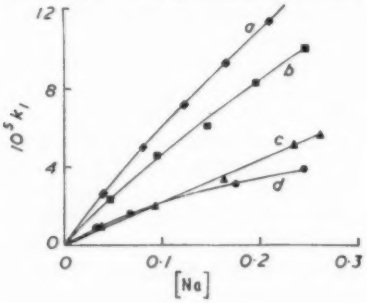
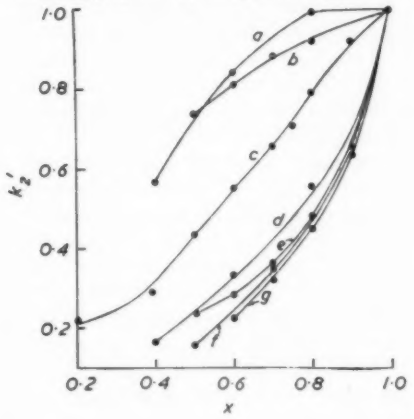


FIG. 2. *Plots of k_2' against x in: a water, b methanol, c ethylene glycol, d ethanol, e 2-ethoxyethanol, f propan-1-ol, and g butan-1-ol.*



in Fig. 3. We attach little significance to the linearity of the plots obtained, for although $k_2 = A + B[\mathrm{ROH}]$, where A and B are constants, A is negative for butan-1-ol. In similar experiments k_2 was found at a constant alcohol concentration with various values of the dielectric constant of the solution (Fig. 4). Again there is little variation in the rate of addition of methanol but a large change for other alcohols. Other experiments showed a negative salt effect for propan-1-ol and butan-1-ol, but the rate of addition of methanol was unaffected by the presence of added salt. In all three cases the reaction took place in the pure alcohol as solvent, and sodium perchlorate was the salt added.

We conclude that the free alkoxide ion is a more effective catalyst than the sodium alkoxide ion-pair (see also ref. 2), and that under our conditions dissociation of the sodium alkoxide is virtually complete only in solutions of sodium methoxide in pure methanol and in methanol-rich mixtures with 1 : 4-dioxan. Other evidence [6-8] about the extent of

* There was no evidence of reaction between the alkoxide and nitrobenzene, although in later experiments on the polymerisation of ethylene oxide in presence of nitrobenzene there was a slow loss of catalyst.

[6] Jones and Hughes, *J. Amer. Chem. Soc.*, 1934, 1197.
[7] Ogston, *Trans. Faraday Soc.*, 1936, **32**, 1679.
[8] Hovorka and Sims, *J. Amer. Chem. Soc.*, 1937, **59**, 92.

dissociation of alkoxides and other salts in solution in alcohols confirms this view. The large decrease in k_2 for reactions in propan-1-ol and butan-1-ol as the dielectric constant falls, at constant alcohol concentration (Fig. 4), is probably due at least in part to a decrease in the degree of dissociation of the catalyst. In methanol solutions, changes in the relatively large dissociation constant of sodium methoxide will little affect the degree of dissociation, which is near unity. For these solutions, the experiments in which the dielectric constant remains the same and the methanol concentration is varied (Fig. 3)

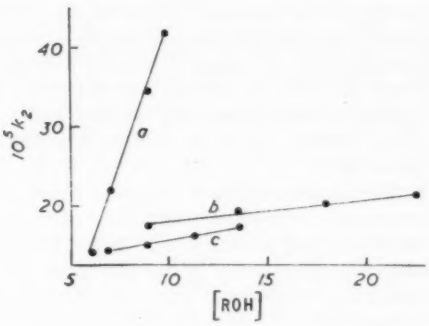


FIG. 3. *Plots of k_2 against* [ROH] *in*: *a butan-1-ol* ($D = 17$), *b methanol* ($D = 29{\cdot}5$), *and c methanol* ($D = 19$).

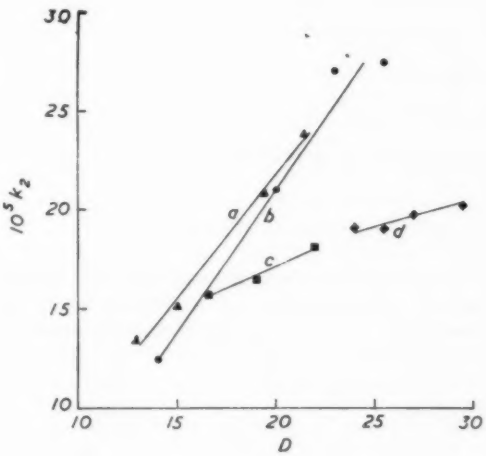


FIG. 4. *Effect of dielectric constant in*: *a butan-1-ol* (7·0M), *b propan-1-ol* (7·3M), *c methanol* (11·2M), *d methanol* (17·9M).

suggest that the alcohol concentration does not enter into the rate equation. If this is also true of other alcohols, the rapid decrease in k_2 with the alcohol concentration, when the dielectric constant is kept the same by addition of nitrobenzene, shows that the degree of dissociation of the catalyst depends upon the nature of the solvent molecules present as well as on the bulk dielectric constant. The alcohols are more effective than nitrobenzene, presumably on account of the strong solvating power of their hydroxyl groups.[9] Finally, the salt effects observed with propan-1-ol and butan-1-ol are probably due mainly to a decrease in the degree of dissociation of the catalyst in the presence of the sodium ions added. Again, the degree of dissociation of sodium methoxide is likely to be little altered.

In their interpretation of the analogous reaction between alkali-metal ethoxides and

[9] Hughes and Hartley, *Phil. Mag.*, **1933**, **15**, 610.

alkyl halides,[10] Acree and his co-workers showed that it is possible to obtain true second-order velocity constants in systems in which the alkoxide is incompletely dissociated. In our case we can write

$$k_1 = k_{(RO^-)}\alpha c + k_{(RONa)}(1 - \alpha)c$$

where $k_{(RO^-)}$ and $k_{(RONa)}$ are the second-order velocity constants for the reaction of the free alkoxide ion and the sodium alkoxide ion-pair, respectively, with ethylene oxide, c is the concentration of the catalyst, and α is its corresponding degree of dissociation. Three parameters are involved in this equation, the two velocity constants and K, the equilibrium constant for dissociation of the ion-pair, which relates α to c. However, for all the systems studied we find that several widely-varying sets of values of these parameters satisfy the equation over the range of values of c employed. For most alcohols this range was small, owing to the low solubility of the catalyst. Further, K and to a less extent the two velocity constants are likely to vary with c. We conclude that it is impossible to evaluate these velocity constants without knowing values for K at appropriate concentrations of the catalyst.

As an alternative attempt to obtain a value of $k_{(RO^-)}$ for the prop-1-oxide ion we investigated the kinetic behaviour of mixtures of propan-1-ol and methanol, the dielectric constant being maintained at 23·0. In such mixtures the degree of dissociation of sodium prop-1-oxide is likely to be near to unity, on account of the high solvating power of the methanol, so that the total concentration of anions can be taken equal to the catalyst concentration c. If k_m' and k_p' are the bimolecular velocity constants for the reaction of ethylene oxide with the methoxide and prop-1-oxide ions, respectively, in the mixed solvent and k_2 is the observed second-order velocity constant, then

$$k_2 c = k_m'[MeO^-] + k_p'[Pr^nO^-]$$

whence

$$k_2 = k_m' + (k_p' - k_m')[Pr^nO^-]/([MeO^-] + [Pr^nO^-])$$

Since the acid dissociation constant of methanol is 8·0 times greater than that of propan-1-ol,[11] it follows that

$$k_2 = k_m' + (k_p' - k_m')[Pr^nOH]/(8{\cdot}0[MeOH] + [Pr^nOH])$$

Taking $k_m' = 19{\cdot}3 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$ when $D = 23$, we use this equation to calculate k_p', the results being summarised in Table 2. The approximate constancy of k_p' so calculated shows that the concentration of propan-1-ol does not enter into the rate equation

TABLE 2.

[MeOH]/[Pr^nOH]	[Pr^nOH] (M)	10^5k_2 (obs.) (l. mole^{-1} sec.$^{-1}$)	[MeO^-]/c	$10^5k_p'$ (calc.) (l. mole^{-1} sec.$^{-1}$)
0·462	9·9	46·7	0·787	148
1·85	5·5	28·8	0·934	169
7·70	2·2	21·4	0·984	150

under these conditions. This confirms our belief that for alcohols other than methanol the large variations in the second-order velocity constant with the concentration of the alcohol are due to the effect upon the dissociation constant of the sodium alkoxide ion-pair, and that the reaction can be regarded as bimolecular.

The average value of $k_p' = 156 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$ may be compared with the lower values found in propan-1-ol at various catalyst concentrations. These results have been analysed on two alternative assumptions: (*a*) that the ion-pair is unreactive and that the dissociation constant K of the ion-pair depends on c; (*b*) that K is independent of c, and

[10] Robertson and Acree, *J. Amer. Chem. Soc.*, 1915, **37**, 1902; Marshall and Acree, *J. Phys. Chem.*, 1915, **19**, 589.

[11] Hine and Hine, *J. Amer. Chem. Soc.*, 1952, **74**, 5266.

the ion-pair is catalytically active. Results of the two calculations, both made by using $k_p' = 156 \times 10^{-5}$ l. mole^{-1} sec.$^{-1}$, are given in Table 3; k_p'' is the velocity constant for the reaction of the ion-pair Pr^{n}ONa.

TABLE 3.

		Assumption (*a*)		Assumption (*b*)		
c (M)	10^5k_2 (l. mole^{-1} sec.$^{-1}$)	α	*K* (mole l.$^{-1}$)	α	*K* (mole l.$^{-1}$)	$10^5k_p''$ (l. mole^{-1} sec.$^{-1}$)
0·040	67	0·430	0·0130	0·202	$2·05 \times 10^{-3}$	44·5
0·125	58·5	0·375	0·0285	0·125	$2·25 \times 10^{-3}$	
0·210	55	0·353	0·0405	0·094	$2·05 \times 10^{-3}$	

It seems likely that the true state of affairs is intermediate between (*a*) and (*b*). In Part II (following paper) we present evidence that the ion-pair MeONa has approximately one-tenth of the activity of MeO$^-$. If a similar ratio holds here, k_p'' is probably 10—15 l. mole^{-1} sec.$^{-1}$. An increase in *K* as *c* increases is to be expected, arising from the greater ionic strength; in very dilute solutions *K* is probably less than 0·010 mole l.$^{-1}$. For comparison, the limiting dissociation constant [7] of potassium ethoxide in ethanol at 25° is 0·0189 mole l.$^{-1}$; a somewhat lower value is probable for sodium prop-1-oxide in propan-1-ol.

Values of k_2 were found at various temperatures from 24·8° to 40·3° in the solvents methanol, propan-1-ol, and butan-1-ol. We find $k_m = \text{antilog}_{10}\ (10·0 \pm 0·6) \exp[(-18{,}000 \pm 800)/RT]$, $k_p = \text{antilog}_{10}\ (7·7 \pm 0·6) \exp[(-15{,}200 \pm 800)/RT]$, $k_b = \text{antilog}_{10}\ (7·0 \pm 0·4) \exp[(-14{,}400 \pm 600)/RT]$ where k_m, k_p, and k_b are the second-order velocity constants for the reaction with ethylene oxide of sodium methoxide, prop-1-oxide, and but-1-oxide respectively in solution in the corresponding pure alcohol. For the reaction in methanol the pre-exponential factor and activation energy quoted are those for the reaction of the free methoxide ion. Since the degree of dissociation of the sodium alkoxide is less than unity in the other alcohols, these parameters can be regarded only as approximate values for the reaction of the free prop-1-oxide and but-1-oxide ions. However, for each alcohol the apparent activation energy found in a 1 : 1 alcohol–1 : 4-dioxan mixture was the same as that in the pure alcohol, although for 50% propanol and 50% butanol the second-order velocity constants were only about one-sixth of the value in the pure alcohol.

Comparison of the reactivity of different epoxides towards a given base is much more straightforward than comparing alcohols. A series of measurements have been made in methanol solution at 29·8°, where we feel it safe to assume that sodium methoxide is completely dissociated. In presence of excess of methanol, the measured second-order velocity constants k_2 are taken to be true bimolecular constants for the reaction between MeO$^-$ and the oxide. Col. 2 of Table 4 records the observed constants.

TABLE 4.

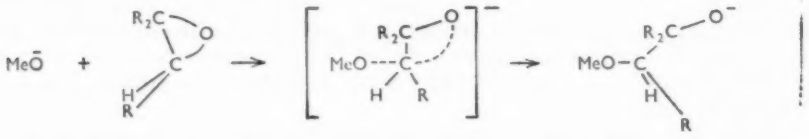
Oxide	10^5k_2	$10^5k_2'$	$10^5k_2''$	$10^5k_2'''$	Oxide	10^5k_2	$10^5k_2'$	$10^5k_2''$	$10^5k_2'''$
	(all in l. mole^{-1} sec.$^{-1}$)								
Ethylene	21·4	10·7	—	—	*trans*-But-2-ene	0·4	—	0·2	—
Propene	11·3	11·0	0·3	—	*cyclo*Hexene ...	1·2	—	0·6	—
*iso*Butene	9·7	9·7	—	0·0	*cyclo*Pentene ...	*ca.* 0·8	—	*ca.* 0·4	—
cis-But-2-ene ...	1·3	—	0·65	—					

In ethylene oxide, two equivalent ·CH_2· groups are available for attack by MeO$^-$. The constant k_2' given in col. 3 of Table 3 is the rate constant for attack at a single ·CH_2· group and is obtained, in the case of ethylene oxide, by halving k_2. Several of the other oxides are symmetrically disubstituted and thus contain no ·CH_2· group but two similar ·CHR· groups. Col. 4 of Table 3 records k_2'', the rate constant for MeO$^-$ + ·CHR·, obtained in these instances by halving k_2.

Interpretation of the total rate constant for an unsymmetrical epoxide requires evidence of the ratio of the rates of attack at the two available points. This was obtained simply

for propene and *iso*butene oxides by submitting the neutralised reaction products to vapour-phase chromatography. The former yielded 97% of the secondary alcohol $CHMe(OH)\cdot CH_2\cdot OMe$, and only 3% of $MeO\cdot CHMe\cdot CH_2\cdot OH$. It is concluded that attack at $\cdot CH_2\cdot$ and $\cdot CHMe\cdot$ is in the ratio 97 : 3, whence the values of k_2' and k_2'' for propene oxide shown in Table 3 were computed. The product from *iso*butene oxide appeared to be exclusively $CMe_2(OH)\cdot CH_2\cdot OMe$. It is concluded that $k_2' = k_2$ and that the rate constant k_2''' for attack at $\cdot CMe_2\cdot$ is too small to be measured by this method.

Table 3 reveals a very simple pattern, in that k_2' and k_2'' are approximately constant. Hence (i) the rate of attack at $\cdot CH_2\cdot$ is not materially changed by substitution at the adjacent carbon atom; (ii) $\cdot CAlk_2\cdot$ is inert. These findings are qualitatively consistent with the nucleophilic nature of the reaction. Attack of MeO^- will be approximately along the line of the C–O bond to be broken:



Alkyl substitution will retard this process by two independent mechanisms: (*a*) inductive transfer of a fractional negative charge to the adjacent carbon atom, (*b*) steric hindrance to the approaching ion. The available evidence is insufficient to indicate which effect is more important in the compounds studied.

Experimental

Epoxides other than ethylene and propene oxides were prepared by treating the corresponding chlorohydrins with alkali, as described for *cyclo*hexene oxide.[12] *iso*Butene chlorohydrin was prepared from 1-chloro-2-methylpropene,[13] *cyclo*hexene and *cyclo*pentene chlorohydrins from the olefins.[14] Samples of *cis*- and *trans*-but-2-ene oxides were kindly presented by Mr. R. Chapman, of these laboratories.

Other reagents were obtained commercially and were purified by conventional methods. The epoxides were dried (CaH_2) and redistilled. 1 : 4-Dioxan was dried by refluxing over sodium metal in the presence of fluorenone as indicator, distilled under nitrogen, and stored in a dark bottle under nitrogen. Alcohols were dried over magnesium metal and distilled.

Catalyst solutions were prepared by dissolving weighed amounts of sodium or potassium metal in the requisite alcohol. In some experiments, the concentration of the catalyst was determined by titration at the end of the experiment and in all cases agreed with the initial values. Initially, reaction mixtures were made up in an all-glass apparatus and the dilatometers were filled in the absence of air. This was later found to be unnecessary, and reaction mixtures were made up by pipette, contact with air being kept to a minimum.

The dilatometers consisted of a 10-ml. bulb to the top of which was sealed a 0·02-cm. diameter graduated capillary of length 30 cm. At the bottom of the bulb a U-tube led *via* a tap to a cylindrical mixing chamber. To avoid leakage through the tap the reaction solution on either side was displaced by mercury immediately after filling the bulb.

In a number of cases, parallel experiments were done in which the concentration of unchanged ethylene oxide was determined by titration, by using the addition reaction with hydrochloric acid.[15] Good agreement was found between velocity constants determined by the two methods. The volume change was not sufficient to require any correction to the concentrations of the reactants.

Manchester University. [*Received, September 26th,* 1958.]

[12] Osterberg, *Org. Synth.*, Coll. Vol. I, 179.
[13] Burgin, Hearne, and Rust, *Ind. Eng. Chem.*, 1941, **33**, 385.
[14] Coleman and Johnstone, *Org. Synth.*, Coll. Vol. I, 151.
[15] Lichtenstein and Twigg, *Trans. Faraday Soc.*, 1948, **44**, 905.

XUM

267. *Polymerisation of Epoxides. Part II.*[1] *The Polymerisation of Ethylene Oxide by Sodium Alkoxides.*

By GEOFFREY GEE, W. C. E. HIGGINSON, and G. T. MERRALL.

The polymerisation of ethylene oxide in solution in 1 : 4-dioxan is catalysed by solutions of sodium in an excess of a simple alcohol, ROH. The dependence of the rate of polymerisation and the molecular weight of the product upon reactant concentrations has been investigated. These experiments support the suggestion that the initiation and propagation reactions are, respectively,

$$RO^-(Na^+) + C_2H_4O \longrightarrow RO{\cdot}C_2H_4O^-(Na^+)$$
$$\text{and } R{\cdot}[O{\cdot}C_2H_4]_n{\cdot}O^-(Na^+) + C_2H_4O \longrightarrow R{\cdot}[O{\cdot}C_2H_4]_{n+1}{\cdot}O^-(Na^+)$$

and that there is no termination reaction. Both the ion-pair, RO^-Na^+, and the ion, RO^-, are catalysts, the reaction of the ion-pair being dominant at low initial concentrations of the conjugate alcohol.

Deviations from the kinetic predictions of this simple scheme are discussed in terms of the relative reactivity and basicity of the anions RO^- and $R{\cdot}[O{\cdot}C_2H_4]_n{\cdot}O^-$.

ETHYLENE OXIDE is conveniently polymerised by bases, and the reaction sequence takes a particularly simple form when an alkoxide ion RO^- is used as initiator:

$$RO^- + C_2H_4O \longrightarrow RO{\cdot}C_2H_4O^-$$
$$RO{\cdot}C_2H_4O^- + C_2H_4O \longrightarrow R{\cdot}[O{\cdot}C_2H_4]_2{\cdot}O^- \text{ etc.}$$

No termination reaction is expected, but a series of proton-exchange reactions arise from the presence of excess of alcohol, usually added to increase the solubility of the catalyst. If, as we expect, these exchange reactions are much faster than the polymerisation, their effect on the kinetics of polymerisation will be negligible unless the alcohol added differs markedly in acid strength from the polyether alcohols. In most experiments now described we used sodium methoxide as catalyst, with a small excess of free methanol. In most cases 1 : 4-dioxan was also present as an inert diluent.

From Part I [1] it is clear that under these conditions the catalyst will be only partially ionised. Moreover, as reaction proceeds, the nature of the solvent changes, especially if no diluent is added, so that the degree of ionisation is not necessarily constant. This effect, together with the small change in the nature of the reacting ions, is likely to cause variations in the velocity constants observed at different stages of the polymerisation. Since it seems scarcely possible to predict the exact quantitative pattern, we begin by assuming that all the polymerisation steps have the same constant rate. Subsequently we shall discuss the extent to which our experimental results show deviations attributable to this over-simplification.

Simple Reaction Scheme.—If each individual reaction has the same bimolecular velocity constant k, the overall rate of reaction is given by

$$-d[C_2H_4O]/dt = k[C_2H_4O]\sum_{n=0}^{\infty}[R{\cdot}[O{\cdot}C_2H_4]_n{\cdot}O^-] \quad . \quad . \quad . \quad . \quad (1)$$

In this form we have implicitly assumed complete ionisation. To be more realistic we should divide $k\sum[R{\cdot}[O{\cdot}C_2H_4]_n{\cdot}O^-]$ into two terms, representing the separate contributions of ions and ion-pairs. So long as the degree of ionisation remains constant, we shall not introduce error by retaining the simple form. Since no ions are formed or lost during the polymerisation, the summation gives simply c_0, the initial concentration of catalyst used, and eqn. (1) reduces to

$$-d[C_2H_4O]/dt = kc_0[C_2H_4O] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

[1] Part I, preceding paper.

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Disappearance of ethylene oxide should therefore follow a first-order law, with a constant proportional to the catalyst concentration.

The presence of alcohol will give rise to the series of reactions

$$R\cdot[O\cdot C_2H_4]_n\cdot O^- + R\cdot[O\cdot C_2H_4]_x\cdot OH \rightleftharpoons R\cdot[O\cdot C_2H_4]_n\cdot OH + R\cdot[O\cdot C_2H_4]_x\cdot O^-$$

where n and x take all integral values from zero to infinity. Since these reactions leave the total ion concentration unchanged, they cannot affect the observed overall rate if our assumption of equal reactivity of all ions is valid. However, the alcohol will affect the molecular weight. Each alcohol molecule, equally with each alkoxide ion, is a potential growing point for a polymer. The total concentration of polymer chains will therefore remain constant during most of the reaction, and equal to $[ROH]_0 + c_0$, where $[ROH]_0$ is the initial alcohol concentration. The number-average degree of polymerisation ν at time t is therefore given simply by

$$\nu = \{[C_2H_4O]_0 - [C_2H_4O]_t\} \div \{[ROH]_0 + c_0\} \quad . \quad . \quad . \quad . \quad (3)$$

where $[C_2H_4O]_t$ represents the concentration of ethylene oxide at time t. This counts each ion and alcohol molecule as a potential chain, so that, in averaging, free alcohol is counted as polymer. The molecular-weight distribution, for a polymerisation following this simple scheme, was worked out by Flory [2] for a system free from alcohol; he showed that a Poisson distribution was to be expected, defined by

$$N_x = \frac{N_m}{(x-1)!}\left(\frac{N_m}{N_c}\right)^{(x-1)} e^{-(N_m/N_c)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where N_x = number of polymer molecules each containing x molecules of ethylene oxide, N_m = total ethylene oxide molecules consumed, and N_c = number of catalyst molecules.

Physically, the reason for this very sharp distribution is that all the polymer chains are present throughout the reaction, competing equally for the ethylene oxide. This condition will still be satisfied in the presence of alcohol, *provided* the proton-exchange reaction is rapid. It is easy to show that eqn. (4) is to be generalised to

$$N_x = N_m \nu^{(x-1)} e^{-\nu}/(x-1)! \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

Summarising, we are led by the simple reaction scheme to three conclusions: (1) first-order disappearance of monomer, with a rate constant proportional to catalyst concentration; (2) a number-average degree of polymerisation given by eqn. (3) and unaffected by temperature or presence of diluent; (3) a Poisson distribution of molecular weight.

Deviations from the Simple Scheme.—Departures from this scheme might be expected from three sources: (*a*) The progressive change in the medium during polymerisation might affect the velocity constants of all the steps. (*b*) The reaction between catalyst and monomer will in general have a rate constant different from that of subsequent steps; differences between the remaining rate constants are likely to be small and will not be further considered. (*c*) If free alcohol is present its acid dissociation constant may be different from that of the polyether alcohols. Formal analysis of these factors is deferred to the Appendix; here we shall discuss only their broad effects.

(*a*) Changes in the velocity constants produced by the changing medium are likely to be independent of degree of polymerisation, so that the only effect to be expected is a departure from first-order behaviour. This will occur progressively during polymerisation and will be more marked in absence of diluent than in its presence.

(*b*) If the initiation process is much faster than propagation, the first step will be virtually complete before any higher polymer is produced, but thereafter polymerisation will proceed as in the simple scheme. Apart from a rapid disappearance of monomer in the early stages, no abnormality will therefore be observed. A slow initiation process will have more serious consequences. There will clearly be an initial period of acceleration

[2] Flory, *J. Amer. Chem. Soc.*, 1940, **62**, 1561.

while catalyst is converted into polymer ion, but additional complication will arise because some chains will now grow considerably before others have started to grow. It is physically obvious that this must broaden the molecular-weight distribution since the late starters have a shortened period of growth. On the other hand, the number-average molecular weight will be unchanged, and in consequence the *weight* average will be somewhat increased.

(*c*) The effect of adding an alcohol whose acid dissociation constant differs from that of the polyether alcohol can be seen by considering the equilibria $ROH + R\cdot[O\cdot C_2H_4]_n\cdot O^- \rightleftharpoons RO^- + R\cdot[O\cdot C_2H_4]_n\cdot OH$. We shall discuss only the case in which the added alcohol is the one whose sodium salt is used as catalyst. If this is a much stronger acid than the polymer alcohol, the equilibrium will be displaced to the right and will therefore tend to prevent the growth of any polymer chains until all the alcohol has been incorporated. If the acid strength of the alcohol is sufficient, the total reaction will be split into two consecutive stages: (i) conversion of all ROH into $RO\cdot C_2H_4\cdot OH$, followed by (ii) a simple polymerisation of C_2H_4O by RO^- in presence of $RO\cdot C_2H_4\cdot OH$. In this case the molecular-weight distribution will be sharp [Poisson type in the limiting case where (i) and (ii) are completely separate]. The effect on the overall rate of disappearance of monomer will depend on the rate of stage (i). If this were fast compared with the subsequent propagation, the initial reaction would be fast. In fact this situation is unlikely to arise, since the ready ionisation of ROH would be associated in general with a *slow* reaction of RO^- with ethylene oxide. These two effects would then reinforce one another to produce a slow initial reaction, accelerating when most of the alcohol has been incorporated.

The converse case of an alcohol which is *less* acidic than the polymer alcohol is likely to be associated with high reactivity of RO^-, which will therefore be converted rapidly into the first adduct $RO\cdot C_2H_4\cdot O^-$. As this will have little tendency to react with ROH, further propagation will follow and extensive polymerisation will occur before all the original alcohol is incorporated. After the early rapid reaction, polymerisation will appear kinetically normal, but the product will have a broader molecular-weight distribution.

Experimental Results.—Most of the results to be described were obtained by a dilatometric technique, checked in a few cases by chemical determination of unchanged ethylene oxide at appropriate intervals. The rather considerable contractions involved (23% in absence of solvent) lead to a minor complication in the apparent kinetic pattern. We assume the rate equation to hold in terms of concentrations: $-d[C_2H_4O]/dt = k[C_2H_4O][\text{catalyst}]$. If V is the volume at time t, N the number of moles of monomer unchanged at time t, and N_c the number of moles of catalyst originally added, this gives $-d(N/V)/dt = kNN_c/V^2$. We assume $V = V_\infty + \alpha N$, where α is a constant and V_∞ the final volume when polymerisation is complete.

Defining $(V - V_\infty)$ as ΔV, we can easily show that the rate equation can be written

$$-d \ln(\Delta V)/dt = kN_c/V_\infty = kc_\infty \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

where c_∞ is the *final* concentration of catalyst. It is assumed that c_∞ differs from c_0 only by reason of the contraction. This assumption has been experimentally verified in most runs. We have also confirmed that the reaction goes to completion, *i.e.*, that no unchanged ethylene oxide remains.

This method of analysis has been used to study changes of temperature and reactant concentrations on the course of the polymerisation. If eqn. (6) holds, a plot of log (ΔV) against t should be linear. The results of two typical experiments are plotted in Fig. 1, in which curve A refers to polymerisation of nearly pure ethylene oxide (1M-methanol added to keep the catalyst in solution), while curve B is more representative of our normal polymerisation procedure, in which monomer was diluted by dioxan. The former displays considerable curvature, while the latter is linear over substantially all of the reaction.

The results of a considerable number of experiments are summarised in Table 1, in which two second-order velocity " constants " are given for each run. The first is derived

from the initial slope of log ΔV *versus* t; the " later " value from the slope at a time equal to twice that required for half the total contraction. The trend shown in Fig. 1 is typical: the velocity constant is usually substantially constant during a reaction except when the initial monomer concentration is high. Moreover, its value is constant over considerable ranges of the concentrations of catalyst (expts. 8—12) and monomer (expts. 2—7). The

FIG. 1.

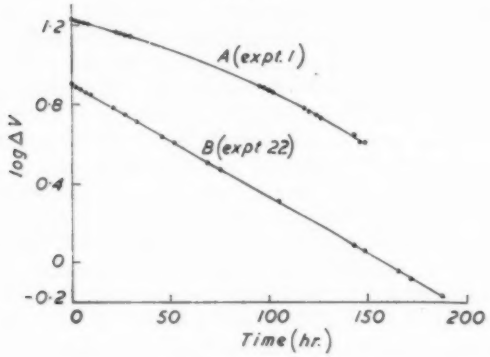
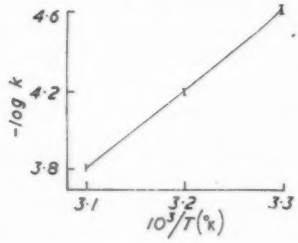


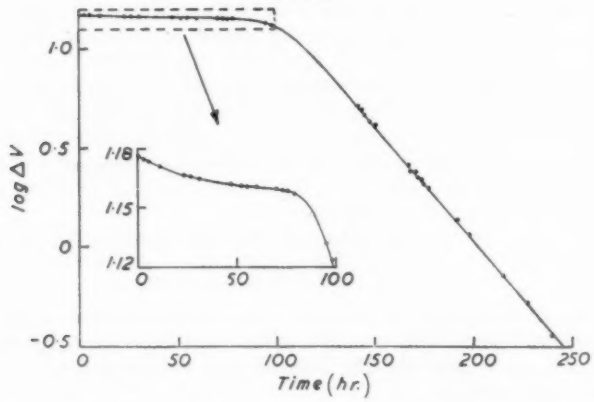
FIG. 2.



second-order constant increases with the methanol concentration as shown by expts. 13—16 (cf. also expts. 17 and 18).

Taking mean values of the initial velocity constants at 30°, 40°, and 50°, including only experiments with $[CH_3 \cdot OH] \simeq 1{\cdot}0$M and with $[C_2H_4O] < 10$M, we have plotted log k against $1/T$ (Fig. 2) and this gives an activation energy of $17{\cdot}8 \pm 1$ kcal. mole^{-1} with a

FIG. 3.



temperature-independent factor of 2×10^8 l. mole^{-1} sec.$^{-1}$. These values are similar to those reported in Part I for the first step.

In a few experiments methanol was replaced by a different alcohol, and some typical results are shown in Table 2: the results do not differ in any important way. Use of phenol (expt. 33) leads to a very different result, shown in more detail in Fig. 3. The slow initial reaction reported by previous workers [3] is fully confirmed (inset to Fig. 3).

An attempt was made to vary the dielectric constant of the medium by addition of

[3] Patat, Cremer, and Bobleter, *Monatsh.*, 1952, **83**, 322.

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1—4M-nitrobenzene, but this led to slow destruction of catalyst, the final concentration being close to zero in each case. Initial polymerisation rates were not markedly affected.

Molecular weights were estimated for most of the polymers obtained and in Tables 1 and 2 these are compared with values calculated from eqn. (3). The experimental values are derived from measurements of intrinsic viscosities in dioxan solution, by using the equation

$$[\eta](\text{ml. g.}^{-1}) = 0{\cdot}083M^{0{\cdot}59} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

This equation was based on viscosity determinations of a series of polyethylene oxide samples kindly supplied by Messrs. Oxirane. Their molecular weights ranged from 300 to 5100 and had been determined by acetylation. Since these materials had been prepared by sodium-catalysed polymerisation, our use of the viscosity method is simply a convenient interpolation procedure to permit of the rapid determination of a large number of molecular weights. Although no high precision is claimed for our figures, the agreement between experimental and calculated values is very striking, and persists through all the changes of temperature and composition. This remained true even though many of the polymerisation tubes were given a final period of heating at 60—80° to accelerate the last few per cent. of reaction.

Discussion

Comparison of our findings with the theoretical analysis presented above shows that most of our results are consistent with the simplest reaction scheme. The molecular-weight evidence, coupled with the observations that all the monomer reacts but no catalyst is lost, shows the absence of either transfer or termination reactions and of polymer–polymer reactions. We have no evidence of molecular-weight distribution, but other workers [4] have analysed low-molecular-weight polyethylene oxides and found their compositions to be consistent with eqn. (5).

Over quite a wide range of conditions, the kinetic behaviour also accords closely with the simple pattern of eqn. (2). The significance of this requires further discussion, and the deviations cannot be ignored. Comparing the two curves in Fig. 1, we attribute the departure from linearity of *A* to large changes in the nature of the medium. After 140 hours' reaction, the concentration of ethylene oxide in *A* is similar to the initial concentration in *B*, but the solvent is a polyether alcohol of average molecular weight *ca.* 600. In the presence of much dioxan as an inert diluent these large changes of medium are avoided.

In the series of expts. 1—7 the initial dielectric constants are estimated to range from *ca.* 13 to 5. None of the experiments reported in Tables 1 and 2 took the dielectric constant outside this range, so this factor does not appear to be important. The effect of alcohol concentration is therefore to be attributed specifically to the hydroxyl groups. In line with the conclusions of Part I, we interpret this in terms of the incomplete dissociation of the sodium alkoxide ion-pair. Evidently, the degree of dissociation of sodium methoxide is small at low methanol concentrations. The constant found at low alcohol concentrations appears to be due mainly to catalysis by the undissociated ion-pair, for if the reaction were due solely to free methoxide ions, the second-order "constant" should depend approximately on the inverse square-root of the catalyst concentration. As shown by expts. 8—12 (Table 1), this is not so. Thus we conclude that at 30° the bimolecular rate constant for $CH_3{\cdot}O^-Na^+$ with ethylene oxide is *ca.* 2×10^{-5} l. mole^{-1} sec.$^{-1}$, which is roughly one-tenth of that for the free methoxide ion reported in Part I.

The simple kinetic behaviour is now seen as a consequence of the fact that most of our experiments have been confined to conditions under which the effective catalyst is an ion-pair, and in which changes in medium during reaction are of little importance. The fact that the initial stages show normal reaction rates demonstrates further that there can be

[4] Miller, Bann, and Thrower, *J.*, 1950, 3623; Weibull and Nycander, *Acta Chem. Scand.*, 1954, **8**, 847.

no major differences of reactivity between the first and subsequent stages.* The strikingly different behaviour of phenol illustrates the consequences of using an acidic compound and follows the pattern predicted by the theoretical analysis.

TABLE 1. *Polymerisation of ethylene oxide in dioxan by sodium methoxide.*

Expt.	Temp.	Initial $[C_2H_4O]$ (M)	100 × Final [NaOMe] (M)	Initial $[CH_3{\cdot}OH]$ (M)	10^5k (l. mole^{-1} sec.$^{-1}$) Initial	Later	Mol. wt. Calc.	Obs.
1	30°	18·6 *	6·95	0·97	2·9	6·0	830	790
2		13·2	6·45	0·97	2·3	3·5	600	590
3		10·6	6·3	0·99	2·6	3·5	475	490
4		8·5	6·1	1·00	2·6	3·0	390	375
5		6·4	5·95	1·00	2·6	2·5	300	285
6		4·8	5·85	1·00	2·6	2·4	230	255
7		3·2	5·7	0·99	2·6	2·3	170	210
8		7·5	11·2	0·77	2·7	3·1	410	470
9		7·5	7·2 †	0·81	2·1	3·8	410	375
10		7·5	5·2	0·83	2·4	2·6	410	380
11		7·5	3·6 †	0·85	2·2	3·6	410	375
12		7·5	2·6	0·85	2·4	2·5	410	355
13		8·7	3·5	0·60	2·3	2·4	635	580
14		8·7	3·7	1·87	3·5	3·3	230	210
15		8·7	3·4	2·52	4·3	4·0	180	170
16		8·7	3·5	3·15	5·1	4·7	150	125
17		4·5	7·2	1·26	3·15	2·8	180	215
18		4·5	7·25	3·46	5·8	5·3	90	—
19	40	10·6	6·35	1·00	6·4	8·8	475	440
20		8·6	6·2	1·00	6·1	7·3	390	375
21		6·5	6·0	1·01	6·4	6·95	300	295
22		4·9	5·9	1·01	6·3	6·35	230	190
23		3·2	5·7	0·99	6·45	6·05	170	170
24	50	6·9	5·35	0·58	15·4	17·2	515	390
25		5·1	5·1	0·57	15·6	17·2	395	460
26		5·1	5·1	1·07	14·8	15·8	230	—
27		5·1	5·1	1·82	17·9	17·7	150	155
28		5·1	5·1	3·07	25·8	25·7	100	60

* No added dioxan. † KOMe catalyst.

TABLE 2. *Effect of variations in alcohol* ($T = 40°$).

Expt.	Initial $[C_2H_4O]$ (M)	100 × Final [NaOR] (M)	ROH	Initial [ROH] (M)	10^5k (l. mole^{-1} sec.$^{-1}$) Initial	Later	Mol. wt. Calc.	Obs.
29	8·6	6·8	MeOH	0·45	5·85	5·85	775	750
30	8·6	9·1	EtOH	0·43	7·2	8·9	790	820
31	8·6	4·7	Pr^{n}OH	0·47	7·5	8·25	805	850
32	8·6	7·5	$MeO{\cdot}C_2H_4{\cdot}OH$	0·44	5·0	8·6	835	930
33	7·9	7·4	PhOH	0·34	0·36	10·0	950	950

Experimental.—Methods and materials were generally similar to those of Part I.[1] The dilatometers were made by sealing a 20-cm. length of graduated tubing of cross-section either 0·25 or 0·13 sq. cm. to a bulb of capacity about 20 ml. A B14 cone sealed to the top of the dilatometer provided connection with a vacuum line or ethylene oxide distillation apparatus. After filling, by pipette or distillation, the contents were frozen in liquid nitrogen and the dilatometer was warmed to room temperature, shaken vigorously to ensure mixing of the contents, and placed in the thermostat.

Molecular weights were determined by diluting the reaction mixture with 1 : 4-dioxan and making viscosity measurements in an Ostwald viscometer, BSS 188, No. 1. It was found unnecessary to extrapolate η_{sp}/c to infinite dilution, values at a relative viscosity of 1·1 being indistinguishable from intrinsic viscosities. In a number of cases the polymer was separated from the reaction mixture by evaporation, and redissolved in dioxan; this procedure gave substantially identical results.

* It is shown in the Appendix that this test is not highly sensitive, so it is difficult to draw quantitative conclusions.

Appendix

Deviations from the Simple Scheme.—If we neglect any effect of chain length on reactivity, the system of reactions to be analysed may be written:

$$C + M \longrightarrow P_1 \qquad \text{velocity constant } \beta k$$
$$P_x + M \longrightarrow P_{x+1} \qquad \text{velocity constant } k \ (x = 1 \text{ to } \infty)$$
$$P_x + HC \longrightarrow P_xH + C$$

where C denotes the alkoxide ion RO^- used as catalyst (concentration c), M is ethylene oxide, and P_x is $R\cdot[O\cdot C_2H_4]_x\cdot O^-$. Writing [P] and [PH] for $\sum_{x=1}^{\infty}[P_x]$ and $\sum_{x=1}^{\infty}[P_xH]$, respectively, we have

$$[P] + c = c_0, \text{ the initial concentration of the alkoxide catalyst} \quad . \quad . \quad . \quad (1)$$
$$[PH] + [CH] = [CH]_0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

We assume the proton exchange to be rapid and write an equilibrium constant K defined by

$$K = c\,[PH]/[CH][P] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

From (1) and (2) this gives $[CH] = [CH]_0 c/\{Kc_0 + (1 - K)c\}$ . . . . . (4)

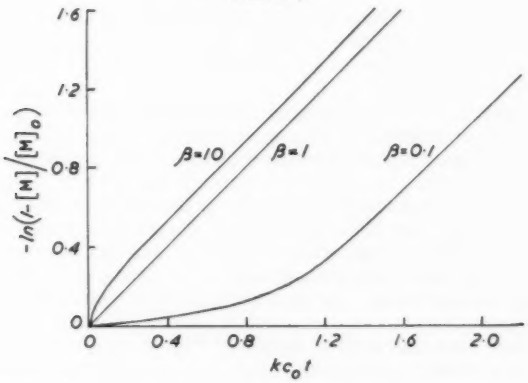
Since the proton exchange does not affect either [M] or the total of $(c + [CH])$ we have:

$$-d[M]/dt = k[M](\beta c + [P]) = k[M]\{c_0 + (\beta - 1)c\} \quad . \quad . \quad . \quad . \quad (5)$$

Since $-d(c + [CH])/dt = \beta k[M]c$, by using (4), we have

$$-\frac{dc}{dt} = \frac{\beta k[M]c\{Kc_0 + (1 - K)c\}^2}{Kc_0[CH]_0 + \{Kc_0 + (1 - K)c\}^2} \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

Fig. 4.



Division of (5) by (6) gives

$$\frac{d[M]}{dc} = \frac{\{c_0 + (\beta - 1)c\}(Kc_0[CH]_0 + \{Kc_0 + (1 - K)c\}^2)}{\beta c\{Kc_0 + (1 - K)c\}^2} \quad . \quad . \quad . \quad (7)$$

which integrates to

$$[M]_0 - [M] = \frac{\beta - 1}{\beta}(c_0 - c) + \frac{\beta K - 1}{\beta} \cdot \frac{[CH]_0(c_0 - c)}{\{Kc_0 + (1 - K)c\}} + \frac{c_0 + [CH]_0}{\beta K} \ln \frac{c_0}{c}$$
$$+ \frac{[CH]_0}{\beta K} \ln \left\{ K + (1 - K)\left(\frac{c}{c_0}\right) \right\} \quad . \quad (8)$$

where $[M]_0$ is the initial concentration of ethylene oxide. This is a generalisation of an equation obtained previously by Bauer and Magat [5] for the special case of $K = 1$, $[CH]_0 = 0$. With the

[5] Bauer and Magat, *J. Chim. phys.*, 1950, **47**, 55.

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aid of (8) it is now possible to integrate eqn. (5) numerically, thus obtaining t and [M] as functions of c. It has been argued that if K is small, β is likely to be large, and *vice versa*. Illustrative solutions have therefore been obtained by setting $\beta K = 1$, which leads to useful simplifications. Writing y for $(1 - c/c_0)$, and z for $(1 - [M]/[M]_0)$, we see that equations (8) and (5) become

$$\frac{[M]_0}{c_0} \cdot z = \frac{\beta - 1}{\beta} y - \left(1 + \frac{[CH]_0}{c_0}\right) \ln (1 - y) + \frac{[CH]_0}{c_0} \ln \left\{1 + y\left(\frac{1}{\beta} - 1\right)\right\} \quad . \quad (9)$$

$$kc_0 \frac{dt}{dz} = \frac{1}{(1 - z)\{1 + (\beta - 1)(1 - y)\}} \quad . \quad . \quad . \quad . \quad . \quad (10)$$

In Fig. 4, $-\ln (1 - [M]/[M]_0)$ is plotted against kc_0t by using data calculated from equations (9) and (10) by putting $\beta = 10$, 1, and 0·1. With $\beta = 1$ the system reduces to the simple form and the reaction follows a first-order plot throughout. It is to be noted that this rate plot is not sensitive to β, especially if $\beta > 1$. The uncertainties inseparable from the early stages of a reaction being borne in mind, β could clearly be considerably greater than 1 without this being obvious from kinetic studies.

MANCHESTER UNIVERSITY. [*Received, September 26th*, 1958.]

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268. *Some Reactions of Cyclopropane and a Comparison with the Lower Olefins. Part IV.* Friedel–Crafts Polymerisation.*

By C. F. H. TIPPER and D. A. WALKER.

Cyclopropane polymerises in heptane between 0° and −78° in the presence of aluminium bromide and hydrogen bromide to give products of low molecular weight (<700). The polymers, whose molecular weight fell with rise of temperature, appeared to be mainly long-chain alkanes with a terminal double bond. A precipitate was formed and there was a continuous loss of aluminium.

The kinetics have been investigated dilatometrically. The rate of polymerisation was a maximum with equal concentrations of $AlBr_3$ and HBr, and was then proportional to the concentrations both of catalyst–cocatalyst and of cyclopropane. The overall activation energy was 6 kcal. mole^{-1}.

The suggested mechanism involves the initial reaction of cyclopropane, aluminium bromide, and hydrogen bromide to give two complexes, one of which initiates the reaction, the other being inactive and precipitated. Propagation, monomer transfer, and termination occurred by the formation of a growing chain–monomer complex, which could rearrange in several ways.

THE lower olefins have been polymerised under a wide variety of conditions with a number of different types of catalyst.[1] In particular Fontana and Kidder [2] found that, in n-butane at −78°, propene rapidly yields polypropene in the presence of aluminium bromide and hydrogen bromide. Ivin [3] studied the mercury-photosensitised reaction of cyclopropane in the gas-phase, and showed that the low polymer formed contained methyl and unsaturated groups and ring structures, but otherwise the polymerisation of this compound has not been reported. However, since cyclopropane readily undergoes the normal Friedel–Crafts reaction with benzene (Part III), it seemed probable that it would polymerise under conditions similar to those of Fontana and Kidder. This has been found to be so, and the kinetics of the reaction and the nature of the products have been investigated.

* Part III, *J.*, 1957, 1199.

[1] Stille, *Chem. Rev.*, 1958, **58**, 541.

[2] Fontana and Kidder, *J. Amer. Chem. Soc.*, 1948, **70**, 3745; *Ind. Eng. Chem.*, 1952, **44**, 1688; Fontana, Herold, Kinney, and Miller, *ibid.*, p. 2955.

[3] Ivin, *J.*, 1956, 2241.

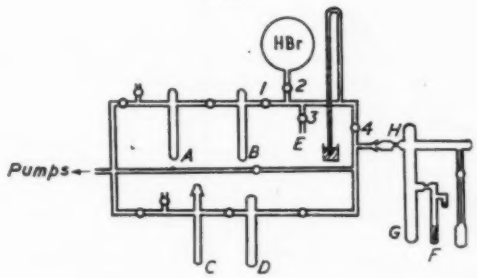
Experimental

Materials.—Traces of substances such as water affect Friedel–Crafts polymerisations, so great care was taken in the purification and handling of all reactants.

The solvent, n-heptane, was washed several times with, successively, concentrated sulphuric acid, sodium hydrogen carbonate solution, and distilled water, and dried with anhydrous sodium sulphate and by refluxing for 24 hr. over sodium. Finally it was fractionally distilled in dry nitrogen, the middle fraction being collected. Gas-chromatography showed that this contained a small proportion of branched isomers. Nitroethane was purified in the same way as nitromethane (Part III). Greenish-yellow commercial aluminium bromide was refluxed and then distilled from pure aluminium chippings in a stream of dry nitrogen into a flask containing more chippings. It was then distilled *in vacuo* into ampoules in approximately 5 g. samples. These were sealed. When required, one was broken *in vacuo* and the solid was distilled into smaller ampoules each containing 0·2 g. of pure white crystalline bromide.

Hydrogen bromide, prepared by the action of bromine on tetrahydronaphthalene,[4] was condensed in a trap and fractionated *in vacuo*, the middle fraction being stored in a blackened bulb attached to the apparatus. Cyclopropane from a cylinder was washed with a solution of mercuric sulphate in sulphuric acid and dried [$CaCl_2$, then $Mg(ClO_4)_2$]. It yielded only one

Fig. 1.



peak when analysed chromatographically. Propene from a cylinder was dried in the same way. " AnalaR " iodine was distilled *in vacuo* into very small ampoules. Conductivity water and " AnalaR " methanol and trichloroacetic acid were not further purified. " AnalaR " toluene was treated as the heptane.

Kinetic Measurements.—The rate of polymerisation was measured dilatometrically. Reactants were mixed and the dilatometer filled *in vacuo* in the apparatus shown in Fig. 1.

The volume between taps 1, 2, 3, and 4 was determined for different levels of mercury in the manometer by means of a flask of known volume attached at *E*. Traps *B* and *D* were graduated in 0·1 ml. Purified cyclopropane (or propene) was condensed in trap *A* and degassed, and a middle fraction transferred to trap *B in vacuo*. *B* was calibrated for use at −78° by distilling out measured volumes of cyclopropane into ampoules immersed in liquid nitrogen. The weights of cyclopropane could then be determined. The effective density was 0·98 g./ml. Purified heptane was placed in trap *C* and a middle fraction transferred to *D in vacuo*.

The dilatometer (vol. ~5 ml.) had a small bulb to allow for expansion at the top of the standard capillary on which a reference mark was scratched. The same dilatometer was used for any one series of experiments. It was cleaned by washing several times with concentrated nitric acid and then with distilled water.

The weighed ampoule containing aluminium bromide (in tube *F*) was broken by a ball-bearing and the contents distilled into tube *G in vacuo*. *F* was sealed off, and the broken ampoule removed and reweighed. A known volume of heptane was distilled *in vacuo* into *G* from tube *D* at room temperature. The bromide was dissolved, and known volumes of hydrogen bromide and cyclopropane were condensed into *G*. If desired, known amounts of water, methanol, or toluene could be added from a graduated trap attached at *E*, or iodine or trichloroacetic acid in the same manner as for the aluminium bromide. When all the reactants were present in *G* it was sealed off at *H in vacuo*, and placed in a bath at −78°, at which temperature the

[4] Mayo and Walling, *J. Amer. Chem. Soc.*, 1949, **71**, 3845.

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reaction was very slow. When the mixture had melted, vigorous shaking produced a clear yellow solution, some of which was then poured into the dilatometer, also at −78°, until it was filled to just below the mark. Since the amount of aluminium bromide could not be controlled exactly, the amounts of the solvent and other reactants were adjusted so that, though the total volume varied, the actual concentrations in *G* and thus in the dilatometer were as required. The dilatometer was sealed off above the expansion bulb and clamped in a standard position in a solid CO_2–alcohol mixture at −78·0° ± 0·1°. When thermal equilibrium was attained the distance between the level of liquid and the reference mark was measured to $\pm 10^{-2}$ mm. with a cathetometer. To determine the rate at higher temperatures the dilatometer was removed to a suitable constant-temperature bath. At various times it was reimmersed in the mixture at −78° and the fall in liquid level measured.

Analyses.—The amount of catalyst remaining in solution during the reaction was found by filtering the mixture and determining the aluminium as the oxide. Added iodine was determined by extracting the reaction mixture with water and titrating the aqueous layer with 0·01N-sodium thiosulphate.

The residue in tube *G* after the dilatometer had been filled was maintained at the reaction temperature long enough for polymerisation to be complete. When *G* was opened, some gas,

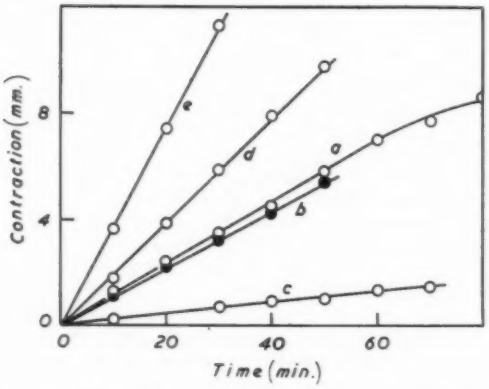


FIG. 2. *Typical results of the dilatometric measurement of the rate of cyclopropane polymerisation.*

a, $[AlBr_3] = [HBr] = 0{\cdot}039$M; [cyclopropane] = 5·4M; temp. = −45·0°.
b, as for (*a*) + 5·4 mole/l. of toluene.
c, $[AlBr_3] = [HBr] = 0{\cdot}039$M; [cyclopropane] = 1·0M; temp. = −45·0°.
d, $[AlBr_3] = [HBr] = 0{\cdot}073$M; [cyclopropane] = 5·4M; temp. = −45·0°.
e, $[AlBr_3] = [HBr] = 0{\cdot}039$M; [cyclopropane] = 5·4M; temp. = −10·0°.

presumably unchanged cyclopropane, was released from solution; the products were then transferred to a separating funnel containing 50% hydrochloric acid. When a number of such residues from experiments under the same conditions had been collected they were extracted several times with the acid, then with water, and the heptane, water, etc., removed *in vacuo* at 100°. The distillate was collected and examined by gas-chromatography after being rigorously dried. The polymer left was dissolved in cyclohexane and precipitated by addition of methanol–concentrated hydrochloric acid. This was repeated several times. Finally solvent was removed *in vacuo* and the molecular weight of the pure polymer determined by the depression of the freezing point of cyclohexane. The infrared spectrum was obtained with a Grubb-Parsons double-beam spectrometer, no solvent being necessary, and the polymer was tested for halides by the Beilstein test.

Results.—Kinetics. The polymerisation of propene being rapid even at −78°, rate measurements were made with cyclopropane only.

A lag of about 20 min. occurred between the filling of the dilatometer and the actual beginning of a kinetic experiment, during which time a pale yellow solid was precipitated. Despite this, the rate of reaction remained constant for at least 50 min., only then decreasing slowly (Fig. 2), and the initial rates were reproducible to within 10% under the same conditions. One set of conditions (curve *a*, Fig. 2) was taken as a reference for all the kinetic measurements, and this reference experiment was repeated before any series was performed.

No reaction took place in nitroethane. With heptane no appreciable reaction occurred at −45° in the absence of hydrogen bromide, and the rate was proportional to the co-catalyst concentration up to a molar ratio of $1AlBr_3 : 1HBr$. Further addition had no further effect (Fig. 3*a*). The rate was also proportional to the concentration of a 1 : 1 $AlBr_3$–HBr mixture

(Fig. 3*b*), and to the cyclopropane concentration except when this was very high (Fig. 4), when the fast rate was difficult to measure since the high proportion of cyclopropane repeatedly broke the thread in the capillary of the dilatometer. The variation of the rate with temperature is shown in Fig. 5. The overall activation energy of polymerisation was 6 ± 1 kcal. mole^{-1}.

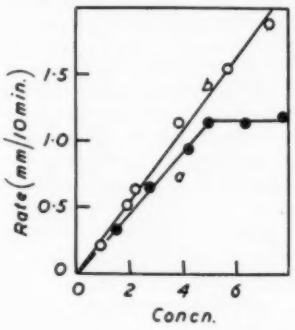


FIG. 3. *Variation of the rate of cyclopropane polymerisation with catalyst concentration.*

[Cyclopropane] = 5·4M; temp. = −45·0°.
a, HBr varied; [$AlBr_3$] = 0·039M.
b, $AlBr_3$ + HBr varied at a constant molar ratio of 1 : 1.
Concn. = 10[HBr]/[$AlBr_3$] + [HBr] *or* 10^2[$AlBr_3$,HBr].

The addition of water, methanol, or trichloroacetic acid to the aluminium bromide–cyclopropane–heptane mixture caused complete inhibition in the presence or absence of hydrogen bromide, a pale yellow oil and a pink precipitate separating with the last two additives respectively. The addition of the same amount of toluene as cyclopropane had little effect on the rate at −45° (Fig. 2), though at room temperature the reaction was extremely rapid.

FIG. 4. *Variation of the rate of polymerisation with concentration of cyclopropane.* [$AlBr_3$] = [HBr] = 0·039M; temp. = −45·0°.

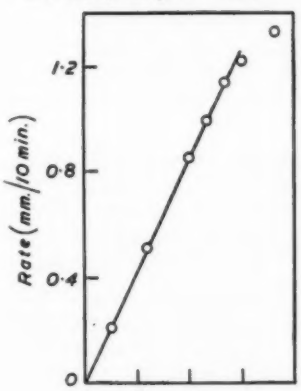
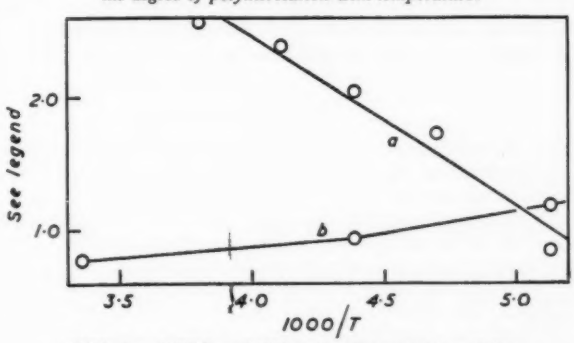


FIG. 5. *Variation of the rate of cyclopropane polymerisation and of the degree of polymerisation with temperature.*



[$AlBr_3$] = [HBr] = 0·039M; [cyclopropane] = 5·4M.
Ordinate: *a*, $\log_{10}$ [Rate (mm./10 min.) + 2]; *b*, $\log_{10}$ D.P.

Iodine retarded the polymerisation, the effect increasing with increasing concentration as shown in Fig. 6.

Analyses. The variation of the concentration of aluminium bromide in the solution as the reaction proceeded is shown in Fig. 7. Precipitation was rapid at first, but the loss of catalyst became much slower as the reaction proceeded. On separation, the precipitate formed a red oil very rapidly at room temperature. The concentration of free iodine fell to zero during an experiment when iodine was added, but the quantitative results were erratic. Whereas the purified heptane or heptane recovered from a solution of aluminium bromide kept at room temperature gave three peaks when analysed chromatographically, the solvent recovered from the reaction mixture was separated into five components, the two new ones

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being lower-boiling hydrocarbons in trace amounts. The polymers were oils whose viscosity increased as the reaction temperature decreased. Under the reference conditions the molecular weight of the polycyclopropane (deep yellow) decreased as the temperature increased (658, 366, and 244 at −78°, −45°, and 25° respectively; degrees of polymerisation D.P. 15·7, 8·7, and 5·8). A plot of $\log_{10}$ D.P. against $1/T$ was not straight (Fig. 5), but the overall activation energy, calculated from the values at the two lower temperatures, since at 25° side reactions probably occurred, was −1·6 kcal. mole^{-1}. Variation of the catalyst concentration had little effect on the molecular weight of the cyclopropane polymer at −45°. The polypropene, which was a very pale straw colour, had M 364 at this temperature.

The infrared spectra of the polycyclopropane exhibited large peaks at 3·49, 6·93, and 7·33 μ, which suggest that it was a paraffinic hydrocarbon, and a band at 13·7—8 μ indicating a methylene chain containing four or more carbon atoms. There was probably little branching. A large peak at 15·6 μ and smaller ones at 9·66 and 11·25 μ showed that there was probably a

FIG. 6.—*Effect of added iodine on the rate of polymerisation of cyclopropane.* [$AlBr_3$] = [HBr] = 0·039M; [cyclopropane] = 5·4M; temp. = −45·0°.

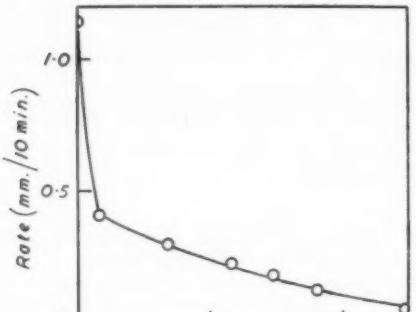
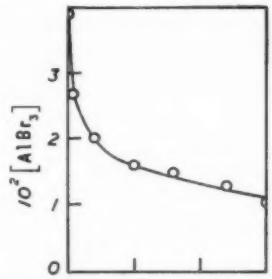


FIG. 7. *Variation of the aluminium bromide concentration in the solution during an experiment.* [HBr] = 0·039M; [cyclopropane] = 5·4M; temp. = −45·0°.



>C=CH_2 end-group. As the temperature increased and the molecular weight of the polymer fell, the bond at 13·7—13·8 μ became less apparent and the peak at 15·6 μ more so. This tends to confirm the structural suggestions above. A peak at 5·88 μ was probably due to a C=O grouping, produced by slight oxygen uptake during extraction of the polymer. The spectrum of the polypropene was not markedly different. None of the polymers gave a positive Beilstein test and therefore bromide was absent.

At −45° the polymer produced in the presence of iodine was a brown oil, M 200. The spectrum was somewhat indeterminate but indicated a paraffinic structure. No peaks were present above about 9 μ and the peak at 5·88 μ was very small. The Beilstein test was positive, and thus it is probable that the product was mainly an alkyl iodide, about $C_6H_{11}I$.

DISCUSSION

Although precipitation occurred, the fact that the rate plots were linear and the rates reproducible indicates that the polymerisation was homogeneous, the precipitate being inactive, but not just catalyst thrown down from a supersaturated solution. The formation of a Friedel–Crafts tar also shows that it contained organic groups as well as aluminium. Fontana and Kidder [2] found that with propene at −78° there was an induction period followed by a rapid rise in rate to a sharp maximum. A white precipitate was formed, and the rate fell to a steady value after which no further precipitation appeared to occur, though no aluminium analyses were reported. Filtering off the precipitate had no effect on the steady rate, and precipitation could be prevented by operating a "semi-continuous" process. If there was an induction period and sharp rate change with

cyclopropane, they could not be observed, owing to the time lag between mixing the reactants and beginning the rate measurements.

The polymerisation of cyclopropane and propene almost certainly proceeds by a carbonium-ion mechanism in a similar way to other Friedel–Crafts polymerisations.[5] Fontana and Kidder [2] found that the kinetics of polymerisation of propene at −78° were very similar to those of polymerisation of cyclopropane reported here except that the dependence on olefin concentration was of the form $[C_3H_6]/(1 + K[C_3H_6])$. They suggested that the rate-determining step was the rearrangement of a growing chain–monomer complex to give a higher carbonium ion:

$$(a)\ M_n{}^+C^- + M \rightleftharpoons M_n{}^+C^-M;\quad (b)\ M_n{}^+C^-M \longrightarrow M_{n+1}{}^+C^-$$

They identified the overall activation energy of 10·3 kcal. mole^{-1} with that of step (*b*) and did not include a termination reaction. They considered that the ionic species was partly precipitated at the beginning of the reaction owing to the non-polar nature of the solvent, but that very soon the solubilising effect of the hydrocarbon chains prevented further loss. The activation energy of the rate-determining growth step seems high for a polymerisation which is rapid at −78°, and at any rate with cyclopropane the results seem to be better explained on the basis of a " normal " type of chain mechanism, especially as not all the monomer was used up when the reaction had stopped.

In order to explain the anomalous effect of hydrogen chloride as cocatalyst on the kinetics of the alkylation of benzene with cyclopropane in the presence of aluminium chloride, it was necessary to postulate the formation of an inactive cyclopropane–catalyst complex (Part III). Thus, since the maximum rate of polymerisation was found with a catalyst–cocatalyst ratio of unity (Fig. 3), it is suggested that the aluminium bromide, hydrogen bromide, and cyclopropane reacted to give two 1 : 1 : 1 complexes. One initiated the polymerisation, and the other was inactive and, since it was ionic, precipitated from the non-polar solvent. It is possible that the first stage was the formation of a π-complex, of the type postulated as the intermediate in the reaction of cyclopropane and lithium aluminium hydride to give tripropylaluminium,[6] followed by addition of HBr in either of two ways leading to splitting of the ring, *viz.*,

$$AlBr_3 + C_3H_6 \longrightarrow C_3H_6\text{-}\pi, AlBr_3 \xrightarrow{HBr} C_3H_7{}^+AlBr_4{}^+ \text{ active}$$
$$C_3H_6\text{-}\pi, AlBr_3 \xrightarrow{HBr} BrC_3H_6{}^+[AlBr_3H]^- \text{ inactive}$$

This is, of course, purely conjectural, though it is likely that n-propyl ions were the original growth centres.

Following Fontana and Kidder,[2] we may suppose that propagation occurred by the formation of a growing chain–monomer complex, which could rearrange to a higher carbonium ion:

$$R{\cdot}CH_2{\cdot}CH_2{}^+AlBr_4{}^- + C_3H_6 \longrightarrow \underset{AlBr_4{}^-\ (A)}{R{\cdot}CH_2{\cdot}CH_2{}^+,\ \pi\text{-}C_3H_6} \longrightarrow R{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{}^+AlBr_4{}^-$$

It is usually assumed that the activation energy of propagation of Friedel–Crafts polymerisation is small,[5] and if the rate of the above process was high then the ion-pairs of lower molecular weight would not have had time to be precipitated. However, since the polymer formed had a low molecular weight and contained terminal double bonds, proton transfer probably also occurred in complex A

$$A \longrightarrow RCH{:}CH_2 + C_3H_7{}^+AlBr_4{}^- \text{ monomer transfer}$$
$$A \longrightarrow RCH{:}CH_2 + BrC_3H_6{}^+(AlBr_3H)^- \text{ termination + precipitation}$$

[5] Pepper, *Quart. Rev.*, 1954, **8**, 88.
[6] Tipper and Walker, *Chem. and Ind.*, 1957, 730.

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In the presence of branched-chain hydrocarbons the molecular weight of polypropene was markedly less than with pure n-butane as solvent, probably owing to hydride-ion transfer to the growing carbonium ions.[2] This transfer may have occurred during the polymerisation of cyclopropane since small amounts of heptane isomers were present, *e.g.*,

$$R{\cdot}CH_2{\cdot}CH_2^+AlBr_4^- + C_4H_9{\cdot}\underset{\displaystyle CH_3}{\underset{|}{C}}H{\cdot}CH_3 \longrightarrow R{\cdot}CH_2{\cdot}CH_3 + C_4H_9{\cdot}\overset{+}{\underset{\displaystyle [CH_3]_2}{\underset{|}{C}}}AlBr_4^-$$

This would account for the traces of hydrocarbons of low molecular weight detected in the solvent after reaction. Further hydride-ion transfer could have led to resonance-stabilised multiply charged carbonium-ion pairs.[2] The presence of these in the precipitate could have been responsible for the colour of the tar formed on warming. The organic part of any extracted with the polymer would have reacted with oxygen giving conjugated groupings responsible for the colour and the peak at 5·88 μ in the infrared spectra. However, hydride-ion transfer was actually of minor importance kinetically, since no appreciable branching was apparent in the polycyclopropane.

The main steps of the polymerisation can be summarised as follows ($M \equiv C_3H_6$, $C \equiv AlBr_3 + HBr$):

1	$M + C \longrightarrow MC$ (active)	Initiation
2	$M + C \longrightarrow CM\downarrow$ (inactive)	
3	$M_nC + M \longrightarrow M_nCM$	Propagation
4	$M_nCM \longrightarrow$ (*a*) $M_{n+1}C$ or (*b*) $M_n + MC$	Propagation
5	$M_nCM \longrightarrow M_n + CM\downarrow$	Termination

If the initial rate measured represented the rate of loss of cyclopropane then, since the loss by reaction 2 was negligible compared with that by 3:

$$\text{Rate} \propto -d[C_3H_6]/dt = k_3[M_nC][M].$$

Despite the relatively small degree of polymerisation, since monomer transfer was important:

$$k_3[M_nC][M] = k_4[M_nCM]$$

at least to a first degree of approximation. If there was a stationary concentration of the complex M_nCM then

$$k_1[M][C] = k_5[M_nCM]$$
$$-d[C_3H_6]/dt = k_1k_4[M][C]/k_5 \propto \text{Rate}$$

as found experimentally. On this basis $E_1 + E_4 - E_5 = 6$ kcal. mole^{-1} and D.P. $= k_{4,a}/[k_{4,b} + k_5]$. Thus $E_{\text{D.P.}} = -1{\cdot}6 = E_{4,a} - E_{4,b}$ or $E_{4,a} - E_5$, depending on whether chain-transfer or termination was the more important factor in determining the length of the polymer chains. This is of course not known, but if $E_{4,a}$ was very small, as seems probable, then $E_1 \approx 5$—10 kcal. mole^{-1}, which is not unreasonable for the activation energy of initiation.[5]

The results with added iodine suggest that it was very effective in terminating the chains, probably by the reaction

$$6M_nCM + I_2 \longrightarrow M_{n+1}I + I^+AlBr_4^-$$

In this case, for stationary conditions,

$$k_1[M][C] = k_5[M_nCM] + k_6[M_nCM][I_2]$$
$$i.e., \quad -d[C_3H_6]/dt = k_1k_3[M][C]/(k_5 + k_6[I_2])$$

and the experimental dependence of rate on iodine concentration was of this general form. The propagating carbonium ion cannot have reacted with toluene at −45°, but alkylation

probably took place at room temperature as might be expected from the results reported in Part III.

Water, methanol, and trichloroacetic acid are often good co-catalysts for Friedel–Crafts polymerisations.[5] Their ineffectiveness in this case, and the iractual inhibiting action when hydrogen bromide was present, was probably due to the non-polar nature of the solvent. The co-catalysts other than HBr formed strongly bound complexes with aluminium bromide, which in heptane were unreactive towards cyclopropane. Nitroethane and aluminium bromide probably form a complex [cf. $AlCl_3,CH_3{\cdot}NO_2$],[6] preventing polymerisation in this solvent.

One of us (D. A. W.) thanks the University of Liverpool for a post-graduate scholarship.

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THE UNIVERSITY, LIVERPOOL. [*Received, October 22nd,* 1958.]

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269. *Magnetic Studies with Copper*(II) *Salts. Part IV.*[1] *Remarkable Magnetic Behaviour of Copper*(II) *Formate and its Hydrates.*

By R. L. MARTIN and HANNEKE WATERMAN.

Four crystalline derivatives of copper(II) formate have been isolated from aqueous formic acid solutions. They are the known tetrahydrate, the known dihydrate, a royal-blue anhydrous compound, and a tetra-formic acid analogue of the tetrahydrate. Dehydration of the di- and the tetra-hydrate yields two further forms of the anhydrous compound. These modifications have been characterised by *X*-ray diffraction and room-temperature magnetic measurements on powders. Spectrophotometry indicates the ephemeral existence of a blue-green binuclear derivative, $[Cu_2(H{\cdot}CO_2)_4]$, in formic acid solution, which however could not be isolated.

The temperature variation of the magnetic susceptibility has been determined between 80° and 360° K for each of the stable compounds. The dihydrate and the royal-blue anhydrous formate obey simple Curie laws, and have normal moments (*ca.* 1·9 B.M.) which are nearly independent of temperature. The remaining compounds have sub-normal moments which decrease with decreasing temperature. However, their susceptibilities can be fitted to Curie–Weiss laws with large negative values of the Weiss constant ($\theta \simeq -175°$). The most highly hydrated formate, $Cu(H{\cdot}CO_2)_2,4H_2O$ is magnetically concentrated, in marked contrast to the magnetically dilute dihydrate and royal-blue anhydrous formate. The origin of this anomalous magnetic behaviour is sought in terms of its known crystal structure, and a consideration of the potential bonding modes of the formate ion. It is suggested that antiferromagnetic exchange demagnetisation takes place *via* a superexchange mechanism which is novel in that formate ion is functioning as a polyatomic counterpart of monatomic anions, such as fluoride and oxide ions, customarily associated with antiferromagnetism.

Our failure to isolate copper formate in the binuclear form is discussed, with reference to possible factors which may influence the adoption of this particular structure by copper *n*-alkanoates.

BINUCLEAR copper *n*-alkanoates are a unique group of compounds which retain much of their spin paramagnetism in the presence of a direct copper–copper bond,[2] which most probably arises from a lateral overlap of $3d_{z^2}$-orbitals centred on each copper atom.[3] This

[1] Part III, Martin and Whitley, *J.*, 1958, 1394.
[2] Martin and Waterman, *J.*, 1957, 2545.
[3] Figgis and Martin, *J.*, 1956, 3837.

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situation offers an unusual opportunity for direct experimental measurement of the exchange energy associated with a single covalent bond, and values of the order of 1 kcal. mole^{-1} have been obtained.[2,4] In the homologous series of *n*-alkanoic acids, the first member, formic acid, is characterised by unconformable behaviour, so it is of interest to ascertain whether its cupric derivative will inherit the nature of the parent acid.

The literature contains only limited information on cupric formate, but it is well established that it crystallises as a tetrahydrate from aqueous solution, and that a dihydrate can be prepared.

Early attempts (1931) to examine the crystal structures of the two hydrates by *X*-ray methods were made by Kabraji [5] and by Prasad and Mapara.[6] More recently Kiriyama, Ibamoto, and Matsuo published a complete structure for the tetrahydrate on the basis of a single-crystal *X*-ray analysis.[7] This reveals a layer-type structure with two non-co-ordinated water molecules per copper atom hydrogen-bonded between adjacent layers. The basic structural unit (I) is an elongated CuO_6 octahedron, each copper atom being surrounded by four oxygen atoms from four different formate groups in an approximately square configuration (Cu–O = 2·00 and 2·01 Å), and two *trans*-co-ordinated water molecules at a greater distance (2·36 Å) to complete a tetragonally distorted octahedron. Obviously the acetate type binuclear structure is not favoured.

Some ambiguity exists as to the exact value of the room-temperature magnetic moment of copper formate. Bhatnagar *et al.* report [8] the value * $\mu = 1{\cdot}77$ B.M. at 290° K for the anhydrous salt, whereas Amiel [9] quotes $\mu = 1{\cdot}67$ B.M. for the tetrahydrate and $\mu = 1{\cdot}59$ B.M. for the anhydrous compound at comparable temperatures. Our own results [2] substantiate Amiel's observations.

A variety of absorption spectra for copper(II) formate indicate that the binuclear acetate-type structure is not naturally adopted by the formate, either in anhydrous or hydrated forms. Thus paramagnetic absorption of microwaves by both forms produces spectra quite different from those characterising the heavier homologues.[10-13] Similarly, all copper(II) alkanoates except the formate show only one absorption band (at about 1600 cm.$^{-1}$) in the infrared region [14] between 1500 and 2000 cm.$^{-1}$. Again the visible and ultraviolet spectra of the binuclear homologues are characterised by absorption at 3750 Å, which is absent from the spectra of both the aqueous [1] and the crystalline [15] tetrahydrate. Clearly, those factors which favour the binuclear structure for the heavier copper alkanoates are not effective in causing its adoption by copper formate.

The present work was undertaken to elucidate the nature of these factors. First, we attempted the preparation of binuclear copper(II) formate in the hope of comparing its properties with those of the higher homologues. Secondly, we wished to measure the temperature dependence of the susceptibility for the different modifications of copper formate, and to ascertain the origin of the sub-normal room temperature magnetic moment of the tetrahydrate.

* These values are recalculated to match our own data, by including a temperature-independent paramagnetic correction for Cu^{2+} equal to 60×10^{-6} c.g.s., e.m.u. The magnetic moment is then $\mu = 2{\cdot}839[(\chi_M - 60)T]^{\frac{1}{2}}$.

[4] Bleaney and Bowers, *Proc. Roy. Soc.*, 1952, *A*, **214**, 451.
[5] Kabraji, *Ind. J. Phys.*, 1931, **6**, 81, 115.
[6] Prasad and Mapara, *idem*, 1931, **6**, 41.
[7] Kiriyama, Ibamoto, and Matsuo, *Acta Cryst.*, 1954, **7**, 482.
[8] Bhatnagar, Lessheim, and Khanna, *J. Ind. Chem. Soc.*, 1937, **14**, 445.
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[13] Sundaramma, *Proc. Ind. Acad. Sci.*, 1955, *A*, **42**, 292.
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[15] Tsuchida and Yamada, *Nature*, 1955, **176** 1171.

Experimental

Materials.—(a) *Solutions of copper carbonate in formic acid.* If copper carbonate is treated slowly without agitation with a large excess of 90% formic acid, a blue-green solution is obtained, the colour being like that of copper(II) acetate. After a few minutes, the solution becomes blue and crystals separate which vitiate magnetic measurements.

The visible and ultraviolet spectrum of the blue-green solution, recorded between 3250 and 8000 Å with a Cary recording spectrophotometer (Model 11 MS–50), is in Fig. 1 (curve *A*) together with that of copper formate in 35% formic acid–acetone (curve *B*). All attempts to crystallise or precipitate the blue-green compound failed.

(b) *Copper formate tetrahydrate.* The preparation of this compound has been described.[1] It crystallises from dilute aqueous solutions of formic acid in large, light-blue prisms which show excellent cleavage.

Fig. 1. *Visible spectra of copper formate: A, in 90% formic acid–water; B, in 35% formic acid–acetone.*

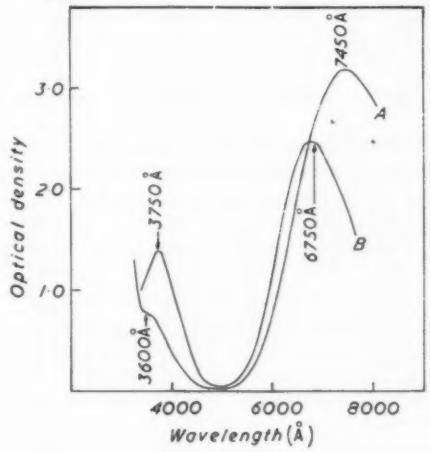
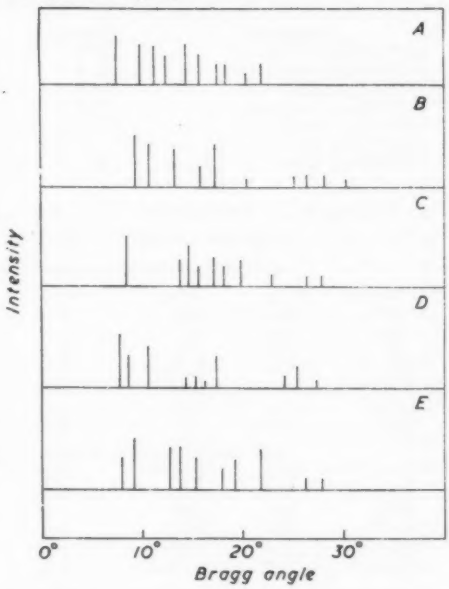


Fig. 2. *X-Ray diffraction of A, copper formate tetrahydrate; B, copper formate dihydrate; C, anhydrous copper formate from the tetrahydrate; D, anhydrous copper formate from the dihydrate; E, royal-blue anhydrous copper formate.*



(c) *Copper formate dihydrate.* This was prepared by rapidly filtering the blue-green solution described in (a) into a large volume of ether (Found: C, 13·0; H, 3·20; Cu, 33·7. Calc. for $CuC_2H_2O_4,2H_2O$: C, 12·7; H, 3·17; Cu, 33·5%). The very pale blue needles of the dihydrate lose water of crystallisation after standing for some hours in air.

(d) *Anhydrous copper formate.* A powder-blue form was readily produced by dehydrating the tetrahydrate for several days over calcium chloride at reduced pressure. As the water of hydration is removed, the crystals become opaque and their faces lustrous, but the external crystal shape is retained (Found: C, 15·6; H, 1·25; Cu, 41·3. Calc. for $CuC_2H_2O_4$: C, 15·6; H, 1·31; Cu, 41·4%).

A pale turquoise modification was obtained by heating the dihydrate at 100° under vacuum over phosphoric oxide. The product again retained the external crystal shape and readily absorbed moisture on exposure to air (Found: C, 15·6; H, 1·51; Cu, 40·9%).

A royal-blue modification, crystallising in small, well-defined rods, was produced when the blue-green solution described in (a) was heated at 100° for several hours. It was formed more

XUM

slowly when the blue-green solution was allowed to stand for several days at room temperature (Found: C, 15·8; H, 1·20; Cu, 41·5%).

(e) *Copper formate–tetraformic acid.* Pale blue plates of copper formate, probably containing four molecules of formic acid, were the initial product deposited from the unstable blue-green solution discussed in (a) when it was kept at room temperature. [After standing for a much longer period, the crystals lose their co-ordinated formic acid and are converted into the royal-blue crystalline anhydrous compound described in (d).] These crystals rapidly decompose as their mother liquor evaporates. Accordingly, the crystals were analysed while still moist (Found: Cu, 17·6. Calc. for $CuC_2H_2O_4,4CH_2O_2$: Cu, 18·8%).

X-Ray Diffraction Photographs.—These were taken of powders of the various modifications of copper formate and its hydrates, a Philips unit type PW1010 and an 11·5 cm. diam. camera being used. The strongest lines are illustrated in Fig. 2, their visually estimated intensities being plotted as a function of Bragg angle. Clearly the five modifications differ fundamentally in their structures.

Magnetic Measurements.—Apparatus and methods described in earlier papers were used. Diamagnetic corrections both for attached groups and for cupric ion were made, and, in

TABLE 1. *Room-temperature magnetic data for copper(II) formates.*

Compound	Temp.	$10^6\chi_g$	$-10^6\Delta$	$10^6\chi_M$	μ (B.M.).
$CuSO_4,5H_2O$ (calibrant)	20·0°	5·90	122	1595	1·91
$Cu(H{\cdot}CO_2)_2$ (royal-blue)	22·6	9·88	48	1566	1·90
$Cu(H{\cdot}CO_2)_2,2H_2O$	18·0	8·00	74	1591	1·90
$Cu(H{\cdot}CO_2)_2$ (turquoise)	18·0	8·52	48	1357	1·75
$Cu(H{\cdot}CO_2)_2,4H_2O$	15·5	4·95	100	1218	1·64
$Cu(H{\cdot}CO_2)_2,4H{\cdot}CO_2H$	17·1	2·87	138	1173	1·61
$Cu(H{\cdot}CO_2)_2$ (blue)	16·2	7·33	48	1174	1·61

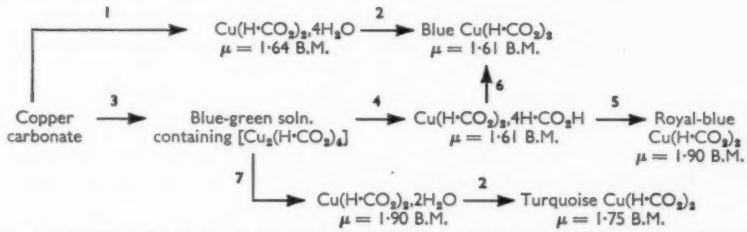
TABLE 2. *Experimental gram and molar susceptibilities (c.g.s., e.m.u.) and magnetic moments (B.M.), at various absolute temperatures.*

Temp. (°K)	$10^6\chi_g$	$10^6\chi_M$	μ (B.M.)	Temp. (°K)	$10^6\chi_g$	$10^6\chi_M$	μ (B.M.)
Anhydrous copper(II) formate: blue modification from tetrahydrate							
82·7	12·0	1897	1·11	184·3	9·11	1448	1·44
89·5	11·9	1877	1·15	212·8	8·50	1353	1·49
95·2	11·8	1867	1·18	245·0	7·90	1261	1·54
101·5	11·8	1853	1·21	272·2	7·39	1182	1·57
108·7	11·5	1816	1·24	291·8	7·10	1139	1·60
125·8	11·0	1743	1·31	304·5	6·94	1113	1·61
154·1	10·2	1618	1·39	333·6	6·48	1043	1·63
Anhydrous copper(II) formate: turquoise modification from dihydrate							
97·3	14·8	2322	1·33	227·5	9·98	1581	1·67
111·4	13·9	2183	1·38	258·6	9·34	1482	1·72
130·4	13·1	2060	1·45	290·5	8·48	1350	1·74
146·7	12·5	1968	1·50	314·5	8·25	1316	1·78
173·2	11·6	1830	1·57	338·5	7·83	1251	1·80
197·8	10·6	1677	1·61	359·2	7·41	1187	1·81
Anhydrous copper(II) formate: royal-blue crystalline modification							
100·5	31·8	4932	1·99	243·6	12·0	1891	1·90
121·0	25·9	4026	1·97	290·5	9·99	1583	1·89
152·3	19·7	3074	1·92	295·6	9·88	1564	1·89
177·3	16·7	2613	1·91	329·0	8·64	1375	1·87
199·4	14·9	2337	1·91				
Copper(II) formate tetrahydrate							
87·5	9·13	2165	1·22	204·5	6·07	1473	1·53
101·0	8·57	2038	1·27	233·0	5·61	1371	1·57
115·5	8·12	1937	1·32	263·3	5·13	1260	1·60
143·4	7·33	1758	1·40	288·5	4·95	1220	1·64
172·8	6·75	1627	1·48	296·4	4·89	1207	1·66
Copper(II) formate dihydrate							
102·5	23·6	4539	1·92	207·9	11·2	2197	1·89
110·6	21·6	4171	1·91	229·2	9·99	1968	1·88
129·7	18·5	3583	1·92	249·5	9·26	1820	1·88
159·9	14·7	2861	1·90	266·5	8·61	1706	1·88
191·1	12·3	2406	1·90	291·5	8·00	1591	1·90

addition, a correction of 60×10^{-6} c.g.s., e.m.u. for the temperature-independent paramagnetism associated with cupric ion. The room-temperature moments are collected in Table 1, the measurements with copper formate–tetraformic acid being on crystals moistened in the minimum quantity of their mother liquor. The dependence of susceptibility and magnetic moment upon temperature (80—360° K) is listed in Table 2. Each sample was studied at two different field strengths between 5000 and 8000 gauss, the mean of the two susceptibilities being taken.

Discussion

This work reveals that, apart from the tetrahydrate which is well known, several forms of copper(II) formate can be prepared from aqueous formic acid, depending upon the conditions of their isolation. Their interrelation is conveniently summarised by the



Reagents, etc.: 1, Dil. $H{\cdot}CO_2H$. 2, $-H_2O$. 3, Conc. $H{\cdot}CO_2H$. 4, Standing. 5, 100°. 6, $-H{\cdot}CO_2H$. 7, Ether.

annexed scheme. When copper carbonate is dissolved in concentrated formic acid the resulting solution has a blue-green colour, reminiscent of the colour of binuclear copper acetate. This colour persists for several minutes, then changes to blue, and pale blue square plates crystallise. The absorption spectrum, in the visible and ultraviolet regions, of the blue-green solution is characterised by an absorption band at 3600 Å in addition to the usual " copper band " at 7450 Å (Fig. 1). Tsuchida *et al.*[14,15] ascribed the unusual absorption band at 3750 Å, which appears in the spectra of the heavier binuclear copper alkanoates, to the inherent copper–copper linkage, so the present band at 3600 Å provides strong evidence for the existence of binuclear copper(II) formate in solution, most probably in $[Cu_2(H{\cdot}CO_2)_4(H{\cdot}CO_2H)_2]$ molecules with structure (II). Unfortunately measurement of the magnetic moment of the cupric ion in the blue-green solution was impossible, owing to the ephemeral nature of the binuclear derivative, and to the rapid growth of crystals a few minutes after the carbonate has dissolved.

Attempts to stabilise the blue-green solution, and to isolate the binuclear compound (II) by replacing water with acetone, were unsuccessful. However, the resultant particularly well-defined absorption maximum at 3750 Å, coupled with a displacement of the " copper band " from 7450 Å to 6750 Å, suggests that acetone molecules have replaced formic acid (or possibly water) from the terminal positions in structure (II) to form $[Cu_2(H{\cdot}CO_2)_4(CH_3{\cdot}CO{\cdot}CH_3)_2]$ molecules.

The pale blue square plates which crystallise so quickly from the solution are unstable in the absence of their mother liquor. Several copper analyses of crystals still moist indicated that they most probably contained four molecules of formic acid per copper atom. The compound, which has a sub-normal room-temperature magnetic moment (1·61 B.M.) like the tetrahydrate (1·64 B.M.), readily loses formic acid to give the same modification of anhydrous copper formate ($\mu = 1{\cdot}61$ B.M.) as is obtained from the tetrahydrate. Clearly, $Cu(H{\cdot}CO_2)_2,4H{\cdot}CO_2H$, is probably the solvate analogue of $Cu(H{\cdot}CO_2)_2,4H_2O$, which has a particularly open structure. The bulky nature of the formic acid molecule compared with the water molecule could account for the rapid decomposition in the absence of formic acid.

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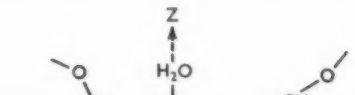
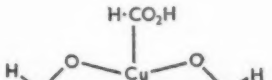
Royal-blue anhydrous copper formate crystallises in well-defined rods when the blue-green solution is heated at 100° for several hours. This modification has a normal magnetic moment (1·90 B.M.), but its insolubility in organic solvents precludes molecular weight, electrical conductivity, or cryoscopic measurements and suggests a polymeric structure. The same compound is also formed when the blue-green solution stands for several days at



(I)

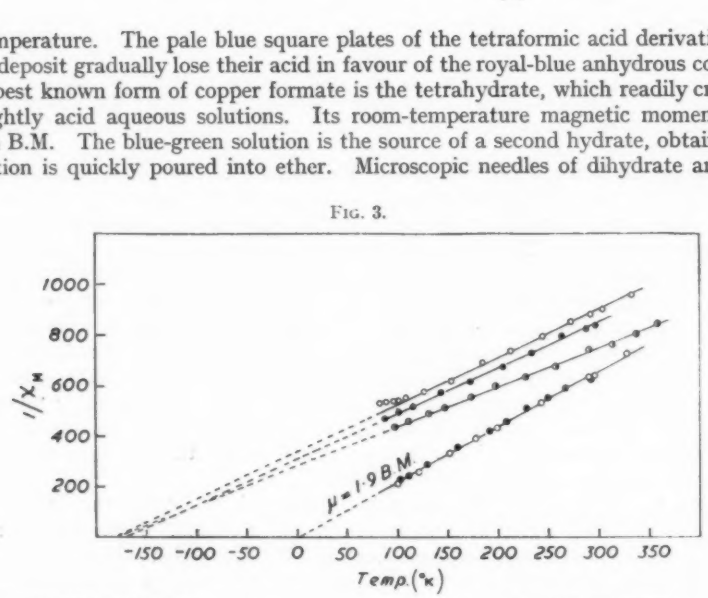


(II)

room temperature. The pale blue square plates of the tetraformic acid derivative which initially deposit gradually lose their acid in favour of the royal-blue anhydrous compound.

The best known form of copper formate is the tetrahydrate, which readily crystallises from slightly acid aqueous solutions. Its room-temperature magnetic moment is low, $\mu = 1{\cdot}64$ B.M. The blue-green solution is the source of a second hydrate, obtained when the solution is quickly poured into ether. Microscopic needles of dihydrate are formed

FIG. 3.



Upper three curves.
○ Dehydrated $Cu(H{\cdot}CO_2)_2,4H_2O$.
● $Cu(H{\cdot}CO_2)_2,4H_2O$.
◑ Dehydrated $Cu(H{\cdot}CO_2)_2,2H_2O$.

Bottom curve.
○ Royal-blue $Cu(H{\cdot}CO_2)_2$.
● $Cu(H{\cdot}CO_2)_2,2H_2O$.

having a magnetic moment as required for one unpaired electron (1·90 B.M.). Both the tetra- and the di-hydrate lose water of crystallisation to form anhydrous salts. The former yields powder-blue opaque crystals ($\mu = 1{\cdot}61$ B.M.) which retain the shape of the parent hydrate, while the latter forms a pale turquoise product ($\mu = 1{\cdot}75$ B.M.). It is unusual to find three inorganic compounds of the same empirical formula. Even so, the different appearances, magnetic properties, and *X*-ray powder diffraction patterns (Fig. 2) leave little doubt that the structures of the three modifications are different. That attempts to isolate a dihydrate by careful dehydration of the tetrahydrate were

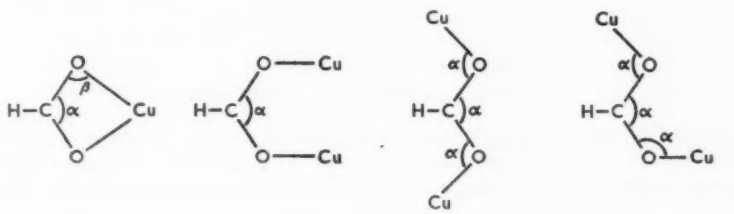
unsuccessful suggests that the dihydrate differs fundamentally in structure from the tetrahydrate.

These compounds fall naturally into two groups on the basis of their magnetic properties. The dihydrate and the royal-blue crystalline anhydrous formate have normal moments which show practically no variation with temperature. Their reciprocal molar susceptibilities vary linearly with temperature, the curves intercepting the temperature axis very close to the origin (Fig. 3). These are magnetically dilute compounds obeying a simple Curie law of the form, $\chi \propto T^{-1}$. In contrast the tetrahydrate, and both the blue and the turquoise form of anhydrous cupric formate, possess sub-normal moments which are strongly dependent on temperature (see Fig. 5). Although their reciprocal susceptibilities vary linearly with temperature, the intercepts of the curves with the temperature abscissa are far from the origin, in the direction of negative temperatures (Fig. 3). These compounds obey Curie–Weiss laws of the form $\chi \propto (T - \theta)^{-1}$ where θ, the Weiss constant, has large values of the order of $-175°$, which is further indication of interaction between the magnetic centres. The marked jump in magnetic moment from 1·61—1·75 to 1·9 B.M. which occurs when the three compounds are dissolved in water [1] further confirms the presence of exchange interactions in the solid state. Although these moments are smaller than those usually observed for magnetically dilute cupric compounds, they are not depressed to the value (1·38 B.M.) observed [2,9] for the heavier binuclear homologues where direct copper–copper intramolecular exchange demagnetisation takes place.

The experimental negation of the rule, so often tacitly assumed, that " the greater the degree of hydration, the greater the magnetic dilution " is noteworthy. Copper formate tetrahydrate, the most highly hydrated formate, is undoubtedly magnetically concentrated compared with both the dihydrate and the royal-blue anhydrous salt.

Clearly it is impossible to establish the origin of these sub-normal moments in the absence of structural information. The present *X*-ray powder diffraction data, while establishing that the various forms of copper formate differ, provide few clues to their actual structures. However, complete crystallographic information is available for the tetrahydrate on which to base an analysis of the magnetic data.

We first consider some of the bonding potentialities of the formate ion. Utilisation of pure *p*-orbitals of oxygen would favour the monomeric chelate structure (III), proposed first by Lowry and French [16] and later by Amiel.[9] Although four-membered rings can



$\alpha = 120°$; $\beta = 90°$.

undoubtedly occur with some chelates, they are generally less stable than five- or six-membered rings, and in the present case considerable steric strain would be present. On the other hand, a pure sp^2-hybridisation of oxygen orbitals would lead to two bonding arrangements, both of which, in contrast to (III), involve one formate group bridging two copper atoms.

[16] Lowry and French, *Proc. Roy. Soc.*, 1924, *A*, **106**, 489.

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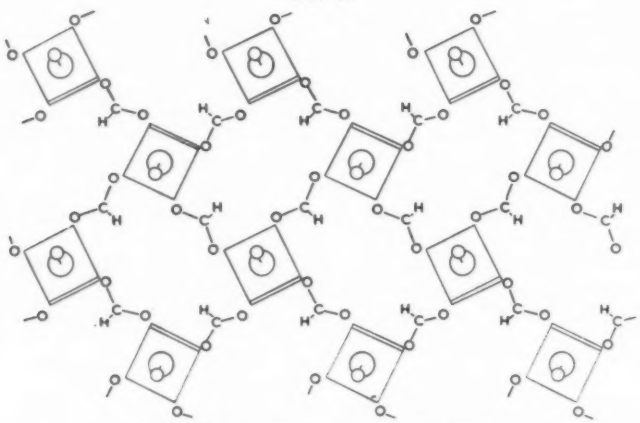
In the first arrangement, two parallel sp^2-hybrid orbitals from the formate oxygen atoms are used to bond two copper atoms, approximately 2·6 Å apart, in a *syn-syn* * bridging arrangement as in (IV). Four such bridging groups are known to support two contiguous copper atoms in binuclear copper(II) acetate monohydrate.[17] In the second arrangement, two opposed sp^2-hybrid orbitals bridge two copper atoms, approximately 5·8 Å apart, in an *anti-anti* bridging arrangement as in (V). A further bonding arrangement based on sp^2-hybridisation of oxygen orbitals would be the *anti-syn* bridging arrangement (VI). The possibility of copper–copper exchange interaction is obvious in the *syn-syn* structure (IV), but is not immediately apparent in the *anti-anti* or *anti-syn* arrangements (V) and (VI).

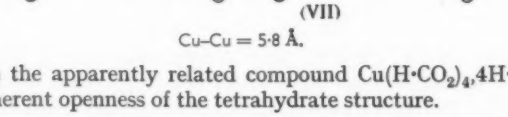
The complete *X*-ray analysis by Kiriyama *et al.*[7] reveals that the layer structure of the tetrahydrate is based on the *anti-anti* bonding arrangement (V). Each layer is very open, and is composed of elongated CuO_6 octahedra (I) which are linked together, in an infinite two-dimensional array, by sharing corners *via* bridging formate groups. Two water molecules co-ordinated to each copper atom lie one above and one below each layer. The CuO_4 planes, formed by the four co-ordinated formate oxygen atoms of each CuO_6 octahedron, do not quite lie in the plane of the copper atoms which provide the framework of each layer. Adjacent octahedra are also slightly rotated contrariwise to one another. The essential structural features of each layer are apparent in Fig. 4.

FIG. 4.



Large circles, copper; small circles, water.

The remaining two water molecules are not linked directly to copper atoms, but are hydrogen-bonded between adjacent layers which are 6·2 Å apart. The easy cleavage, the spontaneous tendency to effloresce, and the possibility of accommodating four molecules of



(VII)

Cu–Cu = 5·8 Å.

formic acid to give the apparently related compound $Cu(H{\cdot}CO_2)_4{,}4H{\cdot}CO_2H$ are all consequences of the inherent openness of the tetrahydrate structure.

* This nomenclature is a convenient extension of that currently employed in organic chemistry to describe the somewhat similar stereochemical configurations which occur in oximes and diazoates.

[17] Niekerk and Schoening, *Acta Cryst.*, 1953, **6**, 227.

The interlayer separation of 6·2 Å precludes direct interlayer exchange interaction, and indicates that the sub-normal magnetic moment originates from magnetic interactions occurring wholly within each layer. At first sight it appears that each copper atom is magnetically well shielded from its nearest copper neighbour at 5·8 Å by the four intervening diamagnetic atoms of each formate group. Closer inspection reveals that the copper atoms form infinite linear chains linked by formate groups, whose C–H bonds approximately bisect the line joining adjacent copper atoms as in (VII). Fig. 4 shows that each copper atom lies at the point of intersection of two such linear chains.

This characteristic recalls corresponding features in the compound $KCuF_3$, in which CuF_6 octahedra share corners to form a distorted perovskite lattice involving infinite linear F–Cu–F–Cu–F–Cu–F chains extending throughout the crystal. Although in this compound also the cupric ions are approximately 5·7 Å apart, *i.e.*, too far for direct interaction, the low room-temperature moment, 1·46 B.M., and the Curie–Weiss temperature-dependence of the susceptibility with a large negative value of θ, almost certainly reflect antiferromagnetic interactions occurring *via* intermediate fluoride ions.[18]

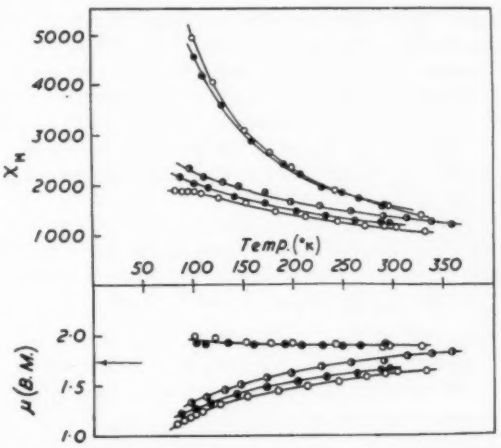


FIG. 5.

Upper curves in each section.
○ Royal-blue $Cu(H{\cdot}CO_2)_2$.
● $Cu(H{\cdot}CO_2)_2,2H_2O$.

Lower curves in each section.
○ Dehydrated $Cu(H{\cdot}CO_2)_2,4H_2O$.
● $Cu(H{\cdot}CO_2)_2,4H_2O$.
◑ Dehydrated $Cu(H{\cdot}CO_2)_2,2H_2O$.

The arrow represents the "spin-only" value of $\mu = 1{\cdot}73$ B.M.

It is suggested that the magnetic anomalies of the tetrahydrate arise from antiferromagnetic exchange interactions between copper atoms through intervening formate groups. If this is correct, then the formate group is functioning in a novel fashion as a polyatomic counterpart of the monatomic ions fluoride, chloride, and oxide which are generally associated with antiferromagnetism.

Antiferromagnetic compounds are characterised magnetically by an angular maximum in their susceptibility–temperature curves, and generally they obey Curie–Weiss laws considerably above the temperature at which the maximum susceptibility occurs (Néel temperature). Spin-aligning forces, acting from one cation to another through an intermediate diamagnetic anion, divide the magnetic ions into two equivalent interpenetrating ferromagnetic sub-lattices. Below the Néel temperature an ordered condition exists in which the spins on one sub-lattice are coupled antiparallel to those on the other; above the Néel temperature, the spins are randomly oriented.

Although the tetrahydrate and the blue and the turquoise modification of anhydrous copper formate, exhibit just those features (sub-normal room temperature moments, temperature-dependent moments, large negative values for θ) which normally characterise antiferromagnetism, susceptibility maxima were not observed down to 80° K. However, an incipient maximum is just evident in the susceptibility curve for the

[18] Martin, Nyholm, and Stephenson, *Chem. and Ind.*, 1956, 83.

dehydrated tetrahydrate (see Fig. 5), which suggests that the Néel temperature should not be very far below 80° K for this compound.

The mechanism by which the spin moment of an electron on one Cu^{2+} cation is coupled antiparallel to the moment of an electron on a neighbouring Cu^{2+} cation separated from it by an intermediate diamagnetic $H{\cdot}CO_2^-$ anion to give rise to antiferromagnetism, is called " superexchange."

In a binary antiferromagnetic compound such as manganese(II) oxide, there is evidence that the interaction between two Mn^{2+} ions is strongest when the bonds to the intervening oxide ion are collinear, and accordingly it has been inferred [19] that the superexchange is principally due to the $2p_\sigma$-electrons of the oxide ion. In contrast, we suggest that in copper formate tetrahydrate the superexchange is primarily due to the delocalised π-electron cloud, which arises from overlapping of $2p_\pi$(O)–$2p_\pi$(C)–$2p_\pi$(O) atomic orbitals associated with the resonating $^-O{-}CH{=}O/O{=}CH{-}O^-$ anion system. This delocalised π-type molecular orbital, which extends over the three nuclei, is believed to provide a low-energy path for migration of electrons * along the infinite linear chains represented in (VII).

Although we regard the delocalised π-electron cloud associated with formate ion as the most likely transmission medium for the postulated superexchange, several other possibilities must be considered. In finding the path of lowest energy for migration of the $3d$-positive electron hole associated with each copper atom, three factors appear of prime importance. They are (*a*) the relative energies of alternative paths offered by each formate ion; (*b*) the " transmission probability " associated with each path, which will be determined by the magnitude of orbital overlap between copper and formate oxygen atoms; (*c*) the relative energies of the ground and excited states of copper under the influence of the ligand field.

The formate ion provides two alternatives for migration of a positive electron hole, either *via* the π-electron cloud, or *via* the σ-bonding electron orbitals of the OCO nuclei. The respective combinations of atomic orbitals appropriate to each path [with axial directions locally defined for each copper nucleus as shown in (I)] are as follows:

$$\pi\text{-path}\quad\begin{cases}(a)\ 3d_{xz}(\mathrm{Cu})\text{–}2p_x(\mathrm{O})\text{–}2p_z(\mathrm{C})\text{–}2p_x(\mathrm{O})\text{–}3d_{xz}(\mathrm{Cu})\\(b)\ 3d_{yz}(\mathrm{Cu})\text{–}2p_z(\mathrm{O})\text{–}2p_z(\mathrm{C})\text{–}2p_z(\mathrm{O})\text{–}3d_{yz}(\mathrm{Cu})\end{cases}$$

$$\sigma\text{-path}\quad\begin{cases}(c)\ 3d_{x^2-y^2}(\mathrm{Cu})\text{–}2sp_\sigma^2(\mathrm{O})\text{–}2sp_\sigma^2(\mathrm{C})\text{–}2sp_\sigma^2(\mathrm{O})\text{–}3d_{x^2-y^2}(\mathrm{Cu})\\(d)\ 3d_{xy}(\mathrm{Cu})\text{–}2sp_\sigma^2(\mathrm{O})\text{–}2sp_\sigma^2(\mathrm{C})\text{–}2sp_\sigma^2(\mathrm{O})\text{–}3d_{xy}(\mathrm{Cu})\\(e)\ 3d_{z^2}(\mathrm{Cu})\text{–}2sp_\sigma^2(\mathrm{O})\text{–}2sp_\sigma^2(\mathrm{C})\text{–}2sp_\sigma^2(\mathrm{O})\text{–}3d_{z^2}(\mathrm{Cu})\end{cases}$$

Utilisation of the σ-path with its high charge localised between oxygen and carbon nuclei would almost certainly be associated with a gross energy barrier. No such restriction would apply to the π-path involving delocalised π-electrons.

Finally, Polder [20] has calculated the ligand-field splittings for the d^9-configurations of octahedrally oxygen-co-ordinated cupric ion, and has shown that with respect to the positive electron hole their stability decreases in the sequence $3d_{x^2-y^2}$, $3d_{z^2}$, $3d_{xy}$, $3d_{xz}$, and $3d_{yz}$, the overall splitting being estimated to be of the order of 21,000 cm.$^{-1}$. Clearly the choice of a σ- versus a π-pathway for the superexchange rests on whether the promotional enery involved in the $3d_{x^2-y^2} \longrightarrow 3d_{xz};3d_{yz}$ transition for copper is greater or less than the energy barrier to mobility of a positive hole offered by the highly localised σ-bonding orbitals of the OCO framework. Although this energy barrier is difficult to estimate, we believe that " preconditioning " copper may well be energetically easier than " preconditioning " the σ-pathway, and accordingly we favour the π-cloud as the probable " transmission medium."

* Careful dehydration of crystalline copper formate tetrahydrate can produce crystal faces which often possess an almost metallic lustre. This may well originate from the delocalized π-electrons which would possess unrestricted mobility throughout the whole of each layer.

[19] Lidiard, *Reports Progr. Phys.*, 1954, **17**, 201.
[20] Polder, *Physica*, 1942, **9**, 709.

The geometric location of a C–H group approximately mid-centre between copper atoms could also conceivably give rise to superexchange through the C–H bonding pair of electrons. This again appears unattractive, for the excited state necessitates a one-electron C–H bond, and the localised nature of the C–H bonding orbital would render favourable overlap with copper 3*d*-orbitals extremely unlikely.

By using Anderson's [21] method of presentation, the interaction scheme associated with the postulated superexchange can be represented in a manner which is independent of which of the above mechanisms is correct. This is illustrated in Table 3.

TABLE 3. *Interaction scheme in superexchange.*

		Cation	Anion	Cation
		Cu^{2+}	$H{-}C(=O)O^{-}$	Cu^{2+}
		3*d*-Orbitals	Interacting orbital involved in superexchange	3*d*-Orbitals
Excited state	singlet	Antiparallel	Spin +ve	Spin −ve
	triplet	Antiparallel	Spin +ve	Spin +ve
Ground state	singlet	Spin +ve	Antiparallel	Spin −ve
	triplet	Spin +ve	Antiparallel	Spin +ve

This scheme qualitatively indicates the process involved in the spin-coupling between formate-bridged cupric ions which gives rise to antiferromagnetic behaviour in copper(II) formate tetrahydrate. In particular, it illustrates that a completely bivalent-ionic description of the molecule as $Cu^{2+}(H{\cdot}CO_2^-)_2$ is inadequate, and that a consideration of other configurations, such as $Cu^{+}(H{\cdot}CO_2)(H{\cdot}CO_2^-)$, can provide a mechanism for superexchange. Further, it illustrates that, contrary to cases in which direct intramolecular exchange between paramagnetic atoms takes place [*e.g.*, $Fe_2(CO)_9$; $W_2Cl_9^{2-}$; $Cu_2(CH_3{\cdot}CO_2)_4(H_2O)_2$], the total spin remains unaltered, so that the effective magnetic moment of cupric ion will not be too greatly diminished by the superexchange coupling.

A study of the magnetic susceptibility of copper(II) formate below 80° K is now needed to test our hypothesis of antiferromagnetism. If an angular maximum in susceptibility is found, the measurements could be profitably extended to single crystals, for the tetrahydrate should be markedly magnetically anisotropic, exhibiting two-dimensional antiferromagnetism in the layer plane but paramagnetism in the direction perpendicular to the layers.

Corresponding structural information is not available for formates other than the tetrahydrate. The retention of external crystalline form on dehydration suggests that the four water molecules are easily removed from between the layers, and that the layers come together without any significant change in the relative orientation of the copper atoms with respect to attached formate groups. If this is so the superexchange within each layer would continue, and account for the persistence of the low room-temperature moment on dehydration of the tetrahydrate. The incipient maximum in magnetic susceptibility which occurs at the lowest temperatures attainable with our apparatus certainly suggests antiferromagnetism (Fig. 5).

[21] Anderson, *Phys. Rev.*, 1950, **79**, 350.

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Any suggestions concerning the magnetic properties of the dihydrate and the two remaining anhydrous modifications are inevitably speculative in the absence of structural data. The cupric ions, in both the royal-blue and the dihydrate structure, are magnetically well shielded from one another, but dehydration of the latter modifies the structure so as to introduce magnetic interactions which are reflected in the decrease in moment from 1·90 to 1·75 B.M. The argument that a moment of 1·75 B.M. is still greater than the spin-only value for cupric ion, 1·73 B.M., and that the decrease does not necessarily indicate a magnetically concentrated compound, is valid, and stresses the weakness of deductions based on a single magnetic measurement at room temperature. Fig. 3 shows that the reciprocal susceptibility curve for the dehydrated dihydrate, quite fortuitously, has the same value of the susceptibility as the parent dihydrate just above room temperature. The slope of its susceptibility curve (proportional to its magnetic moment) is, however, much less than that of the dihydrate. Further, the temperature at which the reciprocal susceptibility becomes zero, changes from zero (Curie law behaviour) for the dihydrate to approximately −175° (Curie–Weiss behaviour) on dehydration. It is these features, rather than the value of the room-temperature moment, which provide significant confirmation of magnetic concentration in the dehydrated dihydrate.

It is of interest to enquire why copper formate differs from its homologues by not adopting the binuclear structure (II) for its stable configuration. Lowering of the total energy by the formation of an extra bond, *i.e.*, the postulated copper–copper δ-bond, can be disregarded, first because its binding energy will be very small, and secondly because it appears to be a consequence, rather than a cause, of the bridged structure. The most obvious difference between the copper derivatives of formic and of other *n*-alkanoic acids is the one between dissociation constants of the parent acids. The heavier alkanoic acids with values of $K_a \simeq 1{\cdot}7 \times 10^{-5}$ are considerably weaker than formic acid with $K_a = 1{\cdot}7 \times 10^{-4}$, reflecting the greater σ-electron density on their hydroxyl-oxygen atoms due to inductive effects of *n*-alkyl groups. As a result, acetate ion, for example, will be more effective than formate ion in reducing the positive charge on the cupric ion in copper alkanoates, and, in fact, it reduces the electrostatic copper–copper repulsion sufficiently for the binuclear configuration to be favoured. On the other hand, with copper formate, the residual positive charge on each cupric ion remains sufficiently large for the *anti-anti* bridging arrangement to be favoured, since it increases the separation between the charged copper atoms from 2·6 to 5·8 Å, and thereby alleviates electrostatic copper–copper repulsion. Consideration of this electrostatic factor alone is an oversimplification; other factors must be taken into account. Even so, it seems that the magnitude of the residual charge on each cupric ion after bonding may well be the most important factor in deciding which of the bonding arrangements (IV) or (V) is likely to be adopted. The question is being pursued.

The authors thank Dr. E. Challen for carbon and hydrogen microanalyses, and Mr. I. H. Reece for assistance with spectrophotometric measurements. They are also grateful to Dr. I. G. Ross for comments. One of them (H. W.) is indebted to the Australian Atomic Energy Commission for a Studentship.

UNIVERSITY OF NEW SOUTH WALES, SYDNEY. [*Received, August 8th,* 1958.]

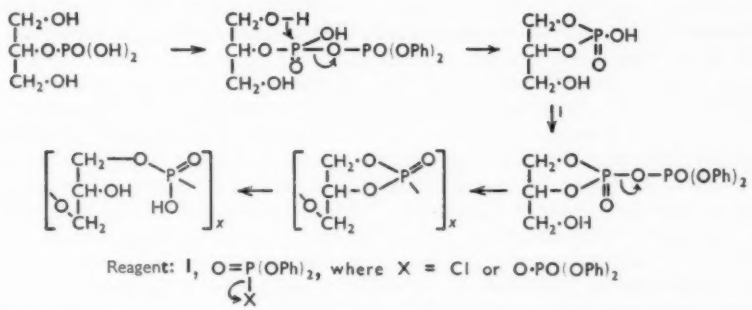
270. *Polynucleotides. Part I. Synthesis and Properties of Some Polyribonucleotides.*

By A. M. Michelson.

Polyglycerophosphoric acid and a number of polyribonucleotides from dimers to fractions with an average chain length ~12 have been prepared from the corresponding monophosphates by the action of diphenyl phosphorochloridate or tetraphenyl pyrophosphate. Chemical and enzymic degradation shows that they are linear polymers analogous to those of natural origin, except that in the polynucleotides some of the linkages are 2′–5′ rather than 3′–5′. The hyperchromic effect, the effect on the light absorption of basic dyes, and changes in dissociation constants shown by the synthetic polynucleotides indicate ordered structures with restricted rotation about the internucleotide linkages. Biological activity is shown by some of the polymers.

Beginning a new approach to the synthesis of polynucleotides we have examined the formation of polymers from, first, glycerophosphoric acid and then the readily available ribonucleoside-2′ or -3′ phosphates.

Treatment of glycerol 2-[mono(tri-*n*-octylammonium) hydrogen phosphate] (or the mixture of 1- and 2-phosphates obtained by phosphorylating glycerol with a limited amount of polyphosphoric acid [1]) with diphenyl phosphorochloridate [2] or tetraphenyl pyrophosphate [3] in the presence of base, a method first used by Forrest, Mason, and Todd [4] for the synthesis of a cyclic phosphate of riboflavin, gave glycerol-1 : 2 cyclic phosphate.[5] Addition of more diphenyl phosphorochloridate, or tetraphenyl pyrophosphate, and tri-*n*-butylamine to the concentrated solution then caused rapid polymerisation, to give a good yield of polyglycerophosphoric acid, isolated as the calcium salt. The course of the reaction, which is essentially an acylation through a mixed anhydride intermediate, may be represented as in the annexed formulæ.



Reagent: I, $O{=}P(OPh)_2$ (X), where X = Cl or $O{\cdot}PO(OPh)_2$

No direct phosphorylation of hydroxyl groups by the diphenyl phosphorochloridate has been observed under the conditions employed, largely because attack at the anion is much faster than at an alcoholic hydroxyl group, most of the reagent being thus consumed immediately. The final cleavage, in aqueous solution, of one of the bonds of the phosphate triester to form the diester can occur in three ways, leading to 1 : 3 glycerol–phosphate linkages, 2 : 3 linkages, or degradation of the polymer. The hydrolysis of uridine-3′ dimethyl phosphate at all pH's (presumably *via* the methyl cyclic phosphate) mainly to

[1] Church, *Proc. Roy. Soc.*, 1864, **13**, 520.
[2] Brigl and Müller, *Ber.*, 1939, **72**, 2121.
[3] Khorana and Todd, *J.*, 1953, 2257.
[4] Forrest, Mason, and Todd, *J.*, 1952, 2530.
[5] Ukita, Bates, and Carter, *J. Biol. Chem.*, 1955, **216**, 867.

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monoesters of uridine-2′ and uridine-3′ phosphate with only a trace of uridine-2′ : 3′ cyclic phosphate [6] indicates that degradation should be slight. Nevertheless this and other considerations will impose a practical limit on the size of polymers which can be prepared by the methods described in this communication.

The crude polymer was a mixture of polyglycerophosphoric acids of different chain lengths, ending in a glycerol cyclic phosphate residue. Dilute acid at room temperature [5] opened this cyclic phosphate to give polymers ending in a phosphate group. Some fractionation was achieved by dialysis, giving a residue with an average chain length of 6·4 glycerol phosphate units. Further dialysis against 2M-sodium chloride gave a final residue (about 20% of the material) with an average chain length of 12·1 units. Paper chromatography indicated that this material contained a considerable amount of higher polymers. Chain length was determined by estimating the inorganic phosphate liberated from the acid-treated polymers by prostatic monoesterase purified by Kerr and Chernigoy's method,[7] the ratio of terminal phosphate to total phosphate giving the average length. Hydrolysis of polyglycerophosphoric acid by 0·1N-hydrochloric acid at 100° caused complete degradation to glycerol, glycerol monophosphates, and glycerol diphosphates. For chromatographic comparison a mixture of glycerol diphosphates was prepared by treatment of glycerol with polyphosphoric acid, followed by acid-hydrolysis; isolation and purification of the product, obtained in good yield, was facilitated through the inverse solubility of the dibarium salt of glycerol-1 : 2(or 3) diphosphate, and final purification was by ethanolic precipitation of the acid barium salt.

Hydrolysis by 0·2N-sodium hydroxide also completely degraded polyglycerophosphoric acid to glycerol and glycerol mono- and di-phosphates. The formation of such products by the action of both acid and alkali is in accord with the general mechanisms advanced by Brown and Todd [8] for the acid-isomerisation of nucleoside-2′ and -3′ phosphates and alkaline degradation of ribonucleic acids. Neither ribonuclease nor the mixture of monoesterase and diesterase present in rattlesnake (*Crotalus atrox*) venom affected the polymers, in agreement with their high specificity. Prostate monoesterase liberated a small amount of inorganic phosphate from the untreated poly(glycerophosphoric acid) owing to partial opening of the terminal cyclic phosphate during working-up. The dephosphorylation of polymers ending in a phosphate group became slower with increase in average chain length.

The synthesis of polynucleotides through the nucleoside cyclic phosphates was even more successful, giving quantitative yields.[9] Dilute solutions of the tri-*n*-octylammonium or tri-*n*-decylammonium salt of the nucleoside-2′(or 3′) phosphate in anhydrous dioxan with slightly more than 1 mol. of tetraphenyl pyrophosphate or diphenyl phosphorochloridate and 2—2·5 mol. of tri-*n*-butylamine yielded the cyclic phosphate quantitatively in one hour at room temperature. Adenosine-2′ : 3′ phosphate and uridine-2′ : 3′ phosphate were thus prepared [10] and isolated as calcium salts. The preparations behaved as single entities on paper chromatography and paper electrophoresis, and were identical in such behaviour with authentic specimens.[11] Acid-hydrolysis yielded the corresponding nucleotides, as did hydrolysis with alkali [11] or prolonged incubation at 37° in a buffer solution at pH 10. While adenosine-2′ : 3′ cyclic phosphate was resistant to ribonuclease, the uridine derivative was converted into the 3′-phosphate.[12]

Further addition of diphenyl phosphorochloridate to a concentrated solution of the nucleoside cyclic phosphate then caused rapid polymerisation. In practice, the cyclic

[6] Brown, Magrath, and Todd, *J.*, 1955, **4396**.
[7] Kerr and Chernigoy, *J. Biol. Chem.*, 1957, **228**, 495.
[8] Brown and Todd, in "The Nucleic Acids," ed. Chargaff and Davidson, Academic Press, New York, 1955, Vol. I, p. 409.
[9] Michelson, *Nature*, 1958, **181**, 303.
[10] Michelson, *Chem. and Ind.*, 1958, 70.
[11] Brown, Magrath, and Todd, *J.*, 1952, 2708; Dekker and Khorana, *J. Amer. Chem. Soc.*, 1954, **76**, 3522.
[12] Brown, Dekker, and Todd, *J.*, 1952, 2715.

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phosphate was generally made in concentrated solution, the reagents being added slowly with stirring in order to prevent precipitation of the nucleotide. Concomitant polymerisation was then unavoidable, and the reaction was completed by the second addition of reagents. The crude product was then precipitated by ether or *cyclo*hexane and purified by precipitation from water as the free acid or the calcium or magnesium salt. Apart from polyuridine-2′(or 3′) phosphate, however, these salts were of little use owing to their very low solubilities in water, particularly with the higher polymers. In this way polyadenylic acid, polyguanylic acid and polyuridylic acid were prepared, as was a co-polymer of the four major monoribonucleotides (adenylic, cytidylic, guanylic, and uridylic acid), which was a synthetic ribonucleic acid similar in many respects to a purified sample of commercial yeast nucleic acid. Polymerisation of mixtures of adenylic and guanylic acids, and of adenylic and uridylic acid, in various proportions gave the mixed polynucleotides, and the versatility of the method was demonstrated by using dilute solutions of the nucleoside-2′ : 3′ cyclic phosphates and allowing the reaction to proceed for a limited time, to give products containing relatively large amounts of smaller oligonucleotides. Co-polymerisation of a mixture of adenylic and uridylic oligonucleotides prepared separately in this way then gave polymer differing from the co-polymerised adenylic and uridylic acids, in that the nucleotides occurred as tracts of purines and pyrimidines rather than in a random fashion. That all of the mixed polymers were truly co-polymers was readily proved by paper electrophoresis.

While co-polymerisation of adenylic and uridylic acid leads to a more or less random distribution of the two nucleotides, some selectivity due to chemical processes may occur. For example, an adenylic–uridylic linkage may be formed in the initial stages more readily than an adenylic–adenylic or uridylic–uridylic linking, owing to the different reactivities of the intermediate phosphate anhydride and of the 5′-hydroxyl groups in the nucleotides. The latter difference would be most significant for guanosine (and possibly cytidine) derivatives, which would tend to appear as the head unit in any chemical co-polymerisation of 2′(or 3′)-nucleotides, or as the tail unit if a 5′-nucleotide derivative were polymerised, owing to the low reactivity of the sugar hydroxyl groups.[13] Adenylic and uridylic acid were chosen to demonstrate the differences between random and non-random distribution because their reactivities were more similar than those of other pairs. However, selectivity may also be caused by π-electron interaction between the bases, so that, while for the moment a random arrangement is assumed, chemical co-polymerisation could, under suitable conditions, lead to a non-random distribution of purines and pyrimidines.

Under the polymerisation conditions generally used, about 20% of the crude product dialysed against water to give a residue with an average chain length of 5—6 nucleotides. Further dialysis against 2M-sodium chloride gave a final dialysis residue (35—40% of the original mixture) with an average molecular weight of 3500—4500. While the average chain length of this fraction was 10—12, the molecular species varied from polymers containing approximately 6 units, to those with up to about 20 nucleotides, and further fractionation should give material of higher average molecular weight. For comparison with the synthetic materials, a specimen of commercial yeast nucleic acid was similarly purified; the ribonuclease-resistant "cores" (*i.e.*, polypurine nucleotides terminating with a pyrimidine-3′ phosphate) were also prepared. Among other products separated from the mixture of oligonucleotides resulting from the action of pancreatic ribonuclease on ribonucleic acid, was the dinucleotide of adenylic and cytidylic acid (A3′P5′C3′P), isolated as the highly crystalline free acid.

The properties of the synthetic polymers indicated that their general structure was analogous to that ascribed to natural oligonucleotides.[8] Mild acid-treatment opened the terminal cyclic phosphate to give polynucleotides with tail units containing a 2′(or 3′)-phosphate. More vigorous acid-degradation gave either purines and/or pyrimidine

[13] Michelson, *Tetrahedron*, 1958, **2**, 333.

nucleoside-2′ and -3′ phosphates depending on the polymer. Aqueous sodium hydroxide caused complete breakdown to the respective mixtures of 2′- and 3′-mononucleotides only; no alkali-stable 5′-phosphorylated material was observed. Treatment with rattlesnake venom gave the expected nucléosides and nucleoside-2′(or 3′) : 5′ diphosphate (the tail nucleotide) [14] after prolonged incubation with rather large quantities of enzyme. Average chain length was determined in all cases by spectrophotometric estimation of the relative amounts of nucleoside and nucleoside diphosphate, paper chromatography or paper electrophoresis being used for the separation. Base ratios of the mixed polymers were likewise determined in this way and by separation of the mononucleotides obtained on alkaline degradation. Where applicable, chain lengths were again determined by removal of the terminal phosphate group by purified prostatic phosphatase. The extremely low solubility of some of the polymers in acid solutions—dissolution is necessary to open the terminal cyclic phosphate—precluded this as a general method, the enzyme preparation being inactive against 2′ : 3′-cyclic phosphates.

While polyadenylic and polyguanylic acid were resistant to the action of pancreatic ribonuclease, some 65% of the internucleotide linkages of polyuridylic acid were cleaved to give a mixture of uridylic acid, and di-, tri-, and tetra-nucleotides containing 2′–5′-linkages exclusively. These oligonucleotides were separated on sheets of paper, and the terminal phosphate group of each was removed with monoesterase to give a series of polyuridylic acids terminating with a nucleoside, that is, U2′P5′U; U2′P5′U2′P5′U; U2′P5′U2′P5′U2′P5′U. The structure and composition of each of these was verified by alkaline hydrolysis to nucleotides and tail nucleoside, estimation of which gave the chain length, confirmed by the ratio of inorganic phosphate liberated by the monoesterase to total phosphate. Spectroscopic examination and determination of total phosphate in the alkaline hydrolysate also gave a molar ratio from which the structure could be determined. While these derivatives were not isolated in the solid state, it is believed that their identity is established.

A mathematical interpretation of the data obtained from the action of ribonuclease on polyuridylic acid is simplified in view of the known specificity of the enzyme. If " A " is a uridine-3′ phosphate unit in the polymer and " B " a uridine-2′ phosphate, then in a chain " n " units long containing " A " in the molar proportion $1 - p$ and " B " in the molar proportion p, fragments of length r can be produced in three ways, if it is assumed that A and B are distributed at random:

(1) When the chain begins $B^{r-1}A$: the probability that a chain begins so is $p^{r-1}(1 - p)$.

(2) Whenever the combination $AB^{r-1}A$ occurs in the chain: the probability of this event for each starting position is $p^{r-1}(1 - p)^2$ for $(n - r)$ possible starting positions, giving a probability that a fragment of length r arises from this cause equal to $(n - r)p^{r-1}(1 - p)^2$.

(3) When the chain ends AB^r. The probability is $p^r(1 - p)$. These probabilities are all independent and the joint probability is:

$$p^{r-1}(1 - p) + p^r(1 - p) + (n - r)p^{r-1}(1 - p)^2 = p^{r-1}(1 - p)\,[1 + p + (n - r)(1 - p)]$$

The proportion by weight of fragments of length r is then:

$$\frac{rp^{r-1}(1 - p)}{n}\,[1 + p + (n - r)(1 - p)]$$

When $1 + p - r(1 - p) = 0$, *i.e.*, $r = (1 + p)/(1 - p)$ and therefore $p = (r - 1)/(r + 1)$, then the expression is independent of " n," that is, the proportion of fragments of length r units is constant, independently of the length of the original chain. From the above

[14] Markham and Smith, *Biochem. J.*, 1952, **52**, 558.

expressions it is possible to calculate the value of p which gives a constant proportion of fragments of given length r, the proportion of r in each case being $rp^{r-1}(1-p)^2$, *e.g.*: $p = \frac{1}{3}, r = 2$; $p = \frac{1}{2}, r = 3$; $p = \frac{3}{5}, r = 4$; etc.

Thus by measuring the proportions of di-, tri-, and tetra-nucleotides formed by the enzyme from fractions of the polymer of different average chain lengths, an estimate of p can be made from the fragment which shows least variation in proportion. The assumption of random distribution of 2′–5′- and 3′–5′-linkages in the synthetic polyuridylic acid may not be valid, as the possibility that formation of a particular linkage depends to some extent on the adjacent linkages cannot be ruled out.

The above expressions may also be applied to ribonucleic acids. For example, if the nucleic acid has a molar ratio of pyrimidines (A) to purines (B) equal to 1, then the proportion of trinucleotide produced by the action of ribonuclease, independently of the state of degradation of the polymer, is $\frac{r(n-r+3)}{n2^{r+1}} = 3/16$ if random distribution occurs, giving a possible method for demonstrating the non-randomness of the purines and pyrimidines in certain ribonucleic acids and biosynthetic copolymers.

When the polymerisation was carried out in dilute solution, products containing relatively large amounts of small oligonucleotides were obtained. Examination of such products from adenosine-2′ : 3′ cyclic phosphate by Dr. L. A. Heppel of the National Institutes of Health, Bethesda, Maryland, indicated the presence of di-, tri-, and tetra-nucleotides terminating with a cyclic phosphate. Treatment of the dinucleotide with dilute acid gave A2′(or 3′)P5′A2′(or 3′)P identical in behaviour on paper chromatography, and with the same electrophoretic mobility, as a biosynthetic specimen of the dinucleotide. Spleen phosphodiesterase [15] split approximately 50% of the material to adenylic acid, the remaining A2′P5′A2′(or 3′)P being resistant to the enzyme. Removal of the terminal phosphate from the dinucleotide by the action of monoesterase gave a mixture of adenosine-2′ adenosine-5′ phosphate and adenosine-3′ adenosine-5′ phosphate, the latter being cleaved by spleen diesterase to adenosine-3′ phosphate and adenosine. (Since the original material had been treated with acid, a process causing isomerisation of internucleotide linkages under certain conditions,[16] the actual proportions of 2′–5′- and 3′–5′-compounds cannot be referred to the dinucleotide mixture obtained from the polymerisation.) Treating the higher polymers of adenylic acid with spleen diesterase yielded products analogous to those obtained by the action of ribonuclease on polyuridylic acid, that is, some mononucleotide, together with enzyme-resistant oligonucleotides containing 2′–5′-internucleotide linkages exclusively. A final point examined by Dr. Heppel [17] was the action of the synthetic polymers as primers for polynucleotide phosphorylase. The synthetic polyadenylic acid greatly stimulated enzymic polymerisation of adenosine diphosphate but was not incorporated into the biosynthetic polymer, as were normal primers containing a free 3′-hydroxyl group available for esterification.

In view of the instability of the terminal cyclic phosphate in oligonucleotides containing such a group, even on storage in the solid state,[18] and since some ring opening was invariably observed in the crude preparations of low molecular weight, causing a somewhat confusing pattern on paper chromatography, no attempt was made to separate the initially formed homologues on a preparative scale. The polyadenylic and polyuridylic acids of low molecular weight were converted into the corresponding oligonucleotides terminating with a 2′(or 3′)-phosphate group by the standard treatment with 0·1N-hydrochloric acid at room temperature. Paper chromatography gave series of adenylic and uridylic oligonucleotides ranging from di- to penta-nucleotide. The structure of each

[15] Heppel and Hilmoe in "Methods in Enzymology," ed. by Colowick and Kaplan, Academic Press, New York, 1955, Vol. II, p. 565.
[16] Brown, Magrath, Neilson, and Todd, *Nature*, 1956, **177**, 1124.
[17] Singer, Heppel, and Hilmoe, *Biochim. Biophys. Acta*, 1957, **26**, 447.
[18] Heppel, personal communication.

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member of the series was determined by the methods previously mentioned and described in detail by Heppel, Ortiz, and Ochoa.[19] Unlike the oligonucleotides obtained by the action of enzymes on polymers of higher molecular weight, the homologues prepared in this way contained both 2′ : 5′- and 3′ : 5′-phosphodiester linkages, as expected. Treatment of each oligonucleotide with prostatic phosphatase gave the corresponding nucleotide derivative containing n nucleosides and $n - 1$ phosphate residues. That the various members described formed a homologous series was further indicated by plotting chain length against log $[(1/R_F) - 1]$, a function of the partition coefficient,[20] for the series $(AP)_n$, $(AP)_{n-1}A$, $(UP)_n$, and $(UP)_{n-1}U$. Straight lines, characteristic of homologous series, were obtained (Fig. 1).

The synthetic polynucleotides having been established as linear polymers containing nucleosides combined through 2′ : 5′- and 3′ : 5′-phosphodiester linkages, the next stage

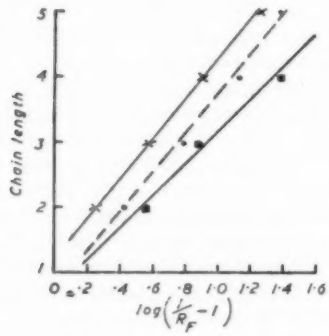

FIG. 1.

× $(UP)_{n-1}U$, ● $(AP)_{n-1}A$, ■ $(AP)_n$

was to prepare polymers with specific head and tail residues. Since ribonucleic acid may be regarded as a polynucleoside-3′ phosphate, or as a polynucleoside-5′ phosphate, depending on whether the terminal phosphate is attached to the secondary or the primary sugar hydroxyl group,[21] it was of particular interest to synthesise oligonucleotides containing a terminal 5′-phosphate. While the obvious route would involve polymerisation of a 5′-nucleotide (or derivative thereof) the success of the present methods encouraged a more circuitous approach.

Treatment of uridine-2′(or 3′) : 5′ diphosphate[22] with excess of diphenyl phosphorochloridate (or tetraphenyl pyrophosphate) yielded P^1-uridine 2′ : 3′-(cyclic phosphate) 5′-(P^2P^2-diphenyl pyrophosphate) quantitatively.[23] Incubation of an aqueous solution at pH 9·5 cleaved the pyrophosphate linkage under conditions such that internucleotide linkages were not broken.[24] Reaction of uridine-2′(or 3′) : 5′ diphosphate and excess of adenosine-2′(or 3′) phosphate in the usual way, followed by the mild pyrophosphorolytic treatment, gave polymers of adenylic acid terminating with uridine-5′ phosphate at the head and adenosine-2′ : 3′ phosphate at the tail. A similar process with uridylic acid gave polyuridylic acid with a terminal 5′-phosphate at one end and a terminal 2′(or 3′)-phosphate at the other, after acid treatment to open the cyclic phosphate. Molar ratios obtained by alkaline hydrolysis to nucleotide and nucleoside-2′(or 3′) : 5′ diphosphate followed by separation and estimation gave a measure of the actual incorporation of 5′-phosphate residue into the polymers. Since ratios of 1 : 10—15 were obtained for material with an average chain length of approximately 7 units, only half of the material actually possessed

[19] Heppel, Ortiz, and Ochoa, *J. Biol. Chem.*, 1957, **229**, 679.
[20] Bate-Smith and Westall, *Biochim. Biophys. Acta*, 1950, **4**, 427.
[21] Todd, *Chem. and Ind.*, 1956, 802.
[22] Hall and Khorana, *J. Amer. Chem. Soc.*, 1955, **77**, 1871.
[23] Michelson, *J.*, 1958, 1957.
[24] Michelson, *Chem. and Ind.*, 1957, 1669.

a terminal 5′-phosphate group. Suitable ratios of the starting materials and alteration of the reaction conditions would probably give more favourable results and, in principle, purification and separation of the smaller oligonucleotides should be possible. The introduction of specific head residues is not limited to nucleosides bearing a 5′-phosphate group; presumably any nucleoside-2′(or 3′) phosphate derivative blocked at the 5′-hydroxyl group would behave similarly and it is clear that polymers terminating with pyrophosphate could be obtained by hydrogenolysis of the diphenyl derivatives.

Attention was then directed to the tail of the molecule. Treatment of uridine-2′ : 3′ cyclic phosphate with diphenyl phosphorochloridate in the presence of excess of benzyl alcohol gave the monobenzyl esters [25] of uridine-2′ and -3′ phosphate as the major products. Hydrolysis with pancreatic ribonuclease [8] indicated that approximately 75% of the mixture was uridine-3′ benzyl hydrogen phosphate, the remaining uridine-2′ benzyl hydrogen phosphate being resistant to the enzyme. In addition to the simple nucleotide benzyl esters, a second product, tentatively identified as a monobenzyl dinucleotide, was also observed. Application to the synthesis of adenosine-2′(or 3′) uridine-5′ phosphate using 2′ : 3′-di-*O*-benzyluridine [26] as the alcohol was not entirely successful, as considerable polymerisation of the adenylic acid occurred in addition to incorporation of the uridine moiety. Further difficulties were encountered in the hydrogenolysis of the benzyl groups, and the preparation was therefore abandoned. More success was obtained with acylation of 3′-*O*-acetylthymidine,[27] the acetyl group being removed from the final products by incubation at pH 9·6 at room temperature for 3 days. The characteristic colour reactions [28] of 2-deoxyribose derivatives facilitated identification of the numerous products shown by paper chromatography; again considerable homopolymerisation occurred in addition to incorporation, even when excess of the thymidine derivative was used. Identification of the homologous series APT, APAPT, APAPAPT was made by the usual methods; these compounds represent a class of nucleotide derivatives not so far found in Nature. A final experiment involved the polymerisation of adenosine-2′(or 3′) phosphate in the presence of both uridine-2′(or 3′) 5′-diphosphate and 2′ : 3′-di-*O*-acetyluridine,[29] followed by very mild alkaline treatment. Although incorporation did occur, to give polyadenylic acid terminating with uridine-5′ phosphate at the head and uridine at the tail, *i.e.*, a polynucleoside-5′ phosphate, this was so only in a statistical sense, and the results are not entirely satisfactory.

In view of the extensive work on the use of mixed anhydrides as synthetical reagents, it was of some interest to examine the action of acid anhydrides other than tetraphenyl pyrophosphate on nucleoside cyclic phosphates. When adenosine-2′ : 3′ cyclic phosphate was treated with *O*-benzylphosphorous *OO*-diphenylphosphoric anhydride,[30] approximately 50% of the adenylic acid was converted into adenosine 2′ : 3′-(cyclic phosphate) 5′-(benzyl phosphite), identified by conversion into a mixture of adenosine-2′ : 5′ and -3′ : 5 diphosphates.[31] The remaining 50% was isolated as polymers containing a 5′-benzyl phosphite group at the head, and a cyclic 2′ : 3′-phosphate at the tail. Average chain lengths of these polymers could not be satisfactorily determined, possibly because of enzyme inhibition, and the polymers were not further examined. Oxidation and hydrogenolysis would presumably give polymers with a terminal 5′-phosphate group. Treatment of uridine-2′ : 3′ cyclic phosphate with methanesulphonyl chloride gave one product only, presumably 5′-methanesulphonyluridine-2′ : 3′ cyclic phosphate (from its behaviour on paper chromatography and paper electrophoresis). Alkaline hydrolysis yielded 5′-methanesulphonyluridine-2′(or 3′) phosphate, isolated as the calcium salt, which showed

[25] Brown and Todd, *J.*, 1953, 2040.
[26] Michelson and Todd, *J.*, 1956, 3459.
[27] *Idem*, *J.*, 1953, 951.
[28] Buchanan, *Nature*, 1951, **168**, 1091.
[29] Kenner, Todd, Webb, and Weymouth, *J.*, 1954, 2288.
[30] Corby, Kenner, and Todd, *J.*, 1952, 3669.
[31] Michelson, *J.*, 1958, 2055.

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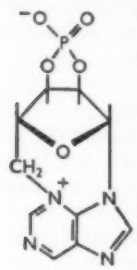
the expected changes in chromatographic and electrophoretic behaviour. No polymerisation was detected. The action of methanesulphonyl chloride on adenosine-2′ : 3′ cyclic phosphate likewise yielded what was presumably the unstable covalent 5′-methanesulphonyl derivative. Heating this intermediate in anhydrous dioxan caused cyclisation to 3 : 5′-*cyclo*adenosine-2′ : 3′ cyclic phosphate (I) which, like the analogous 2′ : 3′-*OO-iso*propylidene-3 : 5′-*cyclo*adenosine toluene-*p*-sulphonate[32] and 2′-deoxy-3′-*O*-acetyl-3 : 5′-*cyclo*adenosine toluene-*p*-sulphonate,[33] showed a bathochromic shift of the ultraviolet absorption maximum from 259 to 272 mμ. As expected, the electrophoretic mobility of this compound was considerably less than that of adenosine-2′ : 3′ cyclic phosphate.



It is well known that the intensity of ultraviolet absorption increases on degradation of a polynucleotide. This hyperchromic effect is relatively large for ribonucleic acid fragments with a high guanine content, and Magasanik and Chargaff[34] suggested that it might be associated particularly with guanylic acid residues, but others

TABLE 1.

Compound	Average chain length	$\lambda_{max.}$ in 0·2N-NaOH Polymer	Products	Alkaline hyperchromicity (%)
Poly U	11·9	261	261	8·6
Poly U	6·6	261	261	6·5
Poly U	3·5	261	261	4·8
Poly A	13·6	257·5	259·5	36·7
Poly A	7·7	258	259·5	31·8
Poly A	3·3	258·5	259·5	19·6
Adenosine-2′(3′) phosphate	—	—	259·5	0
Diadenylic	—	258·5	259·5	15·1
Triadenylic	—	258	259·5	22·8
Tetra-adenylic	—	258	259·5	30·7
Penta-adenylic	—	258	259·5	32·9
Poly G	12·5	260—266	260—266	0
Poly G	5·4	260—266	260—266	0
Poly G	3·2	260—266	260—266	0
A2′P5′U	—	261	260	12·8
A2′(3′)P5′T	—	261	261	12·7
A3′P5′C3′P (from RNAase digest)	—	262	262	7·2
Poly AU (4·5 : 1) Random	5·2	259	260	21·1
Poly AU (4·5 : 1) Random	11·5	—	—	32·0
Poly AU (1·4 : 1) Random	8·3	259·5	261	13·4
Poly AU (1·4 : 1) Random	13·1	—	—	22·0
Poly AU (0·8 : 1) Random	6·8	260	260	9·1
Poly AU (3·1 : 1) Tracts	5·3	259	260	22·9
Poly AU (0·12 : 1) Tracts	4·3	261	261	8·5
Poly AG (2·0 : 1) Random	6·1	258	259·5	19·0
Poly AG (1·9 : 1) Random	3·3	258	260	18·1
Poly ACGU	12·5	—	—	14·3
Poly ACGU	5·2	260	261	11·0
Poly ACGU	3·2	260	261	10·2
Yeast RNA	12·2	—	—	12·0
Yeast RNA	5·1	260	261	12·7
RNAase resistant core	6·2	259	260	10·9
Dialysate	—	262	262	4·7
P5′U poly A	11·9	—	—	32·0
P5′U poly A	6·7	258	259·5	30·5
P5′U poly A	4·0	258	259	23·1
P5′U poly U	5·4	260	261	7·8
P5′U poly U	3·4	260	261	7·7

attributed it mainly to guanylic and cytidylic[35] or polypurine segments.[36] The increase in intensity of ultraviolet absorption at $\lambda_{max.}$ on hydrolysis, by 0·2N-sodium hydroxide at 37°

[32] Clark, Todd, and Zussman, *J.*, 1951, 2952.
[33] Andersen, Hayes, Michelson, and Todd, *J.*, 1954, 1882.
[34] Magasanik and Chargaff, *Biochim. Biophys. Acta*, 1951, **7**, 396.
[35] Mihalyi, Bradley, and Knoller, *J. Amer. Chem. Soc.*, 1957, **79**, 6387.
[36] Reddi, *Biochim. Biophys. Acta*, 1958, **27**, 1.

for 24 hr., then at 20° for 24 hr., of a number of nucleotide derivatives is recorded in Table 1. Appreciable hyperchromic effects were obtained even for dinucleotides, in agreement with observations by de Garilhe and Laskowski [37] and by Sinsheimer [38] on oligodeoxynucleotides from natural sources. The low values for the dialysable products obtained from ribonucleic acid by ribonuclease are due largely to the fact that a considerable proportion of this material is mononucleotide.

The results, and those of de Garilhe and Laskowski,[37] show that the effect is a function, not of any particular tract of nucleotides, but of the total molecule, determined not only

TABLE 2.

Compound	0·01N-HCl	Hyperchromicity in H_2O at pH 7	0·2N-NaOH
Diadenylic	0	—	15·1
Triadenylic	6·8	—	22·8
Tetra-adenylic	13·2	—	30·7
Penta-adenylic	16·4	—	32·9
Polyadenylic (13·6)	22·9	—	36·7
Polyguanylic (3·2)	9·0	10·3	0
Polyguanylic (5·4)	14·6	16·5	0
Polyguanylic (12·5)	18·0	23·0	0
Poly AG (6·2)	14·7	36·7	19·0
A2′P5′U	12·3	16·0	12·8
Polyuridylic (3·5)	4·8	—	4·8
Polyuridylic (6·6)	7·5	—	6·5
Polyuridylic (11·9)	7·5	—	8·6

by the composition but also by the order of bases in the polymer. The influence of chain length is shown in the polyadenylic acid series, where a limiting value of 35% is reached at chain lengths of 5—6. Since polyguanylic acid showed an unexpected zero hyperchromicity, the variation of hyperchromicity with pH was examined (Table 2). The

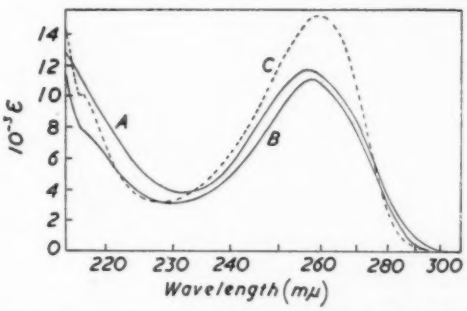


FIG. 2. *Polyadenylic acid (average chain length 13·6 units). A, in 0·01N-HCl; B, in 0·01N-NaOH; C, alkaline hydrolysis products in 0·2N-NaOH.*

effect of pH also varies both with the molar ratios of the bases and their distribution. Some full spectra are reproduced in Figs. 2—4. In water at pH 7, the spectrum of polyadenylic acid (13·6) was virtually identical with the alkaline spectrum (H_2O, $\lambda_{max.}$ 257·5 mμ, ε 10,750; $\lambda_{min.}$ 229·5 mμ, ε 3000), but that of polyuridylic acid (11·9) in water at pH 7 was identical with the acid spectrum ($\lambda_{max.}$ 260·5 mμ, ε 9400; $\lambda_{min.}$ 231 mμ, ε 2300). The hypochromicity of many of the polymers may be readily determined by comparing the ε values [39] with those of the mononucleotides (cf. Table 3). Good agreement with the hyperchromicities determined experimentally by degradation of the polymers was obtained in such cases.

Unlike the case with biosynthetic polymers of high molecular weight,[40] there was no

[37] de Garilhe and Laskowski, *J. Biol. Chem.*, 1956, **223**, 661.
[38] Sinsheimer, *J. Biol. Chem.*, 1954, **208**, 445.
[39] Chargaff and Zamenhoff, *ibid.*, 1948, **173**, 327.
[40] Warner, *ibid.*, 1957, **229**, 711.

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TABLE 3.

Compound	Average chain length	0·01N-HCl $\lambda_{max.}$ (mμ)	0·01N-HCl $10^{-3}\varepsilon$	0·01N-HCl $\lambda_{min.}$ (mμ)	0·01N-HCl $10^{-3}\varepsilon$	0·01N-NaOH $\lambda_{max.}$ (mμ)	0·01N-NaOH $10^{-3}\varepsilon$	0·01N-NaOH $\lambda_{min.}$ (mμ)	0·01N-NaOH $10^{-3}\varepsilon$
Poly U	11·9	260·5	9·4	231	2·3	260	7·15	242	5·9
Poly U	6·6	260·5	9·4	230·5	2·1	260	7·25	242	5·9
Poly U	3·5	260·5	9·54	230	2·2	260	7·3	242	5·9
Poly A	13·6	256·5	11·72	232	3·8	257·5	11·05	229	3·1
Poly A	7·7	256·5	12·75	231	3·65	257·5	11·75	228	2·9
Poly A	3·3	257	13·8	230	3·4	258	12·65	228	3·0
Adenosine-2′(3′) phosphate	—	257	14·4	229	3·2	259·5	15·1	227	2·6
Diadenylic	—	—	14·25 *	—	—	258·5	13·1	229	2·9
Triadenylic	—	—	13·3 *	—	—	258	12·3	229·5	3·0
Tetra-adenylic	—	—	12·54 *	—	—	258	11·5	230	2·9
Penta-adenylic	—	—	12·22 *	—	—	258	11·4	231	2·7
Poly G	12·5	257	10·1	229	2·85	261	11·1	232	4·6
Poly G	5·4	257	10·5	229	2·9	260—265	11·1	232	4·3
Poly G	3·2	257	11·0	229	3·0	260—266	11·1	232	4·3
A2′P5′U	—	258	21·8	231	5·6	261	20·0	236	8·8
A3′P5′C3′P (from RNAase digest)	—	266	—	235	—	262	—	232	—
Poly AU (4·5 : 1)	5·2	257	11·6	230·5	3·1	259	10·55	230	3·25
Poly AU (1·4 : 1)	8·3	258	10·75	230	2·8	259	9·65	233	4·3
Poly AU (0·8 : 1)	6·8	258	11·1	230	2·8	259	9·8	234	5·0
Poly AU (3·1 : 1)	5·3	258	12·7	230	3·2	259	11·1	230	3·9
Poly AU (0·12 : 1)	4·3	260	9·95	230	2·4	260	8·1	240	5·9
Poly AG (2·0 : 1)	6·1	257	12·0	230	—	258	11·6	230	—
Poly ACGU	5·2	258	10·2	230·5	3·5	260	9·9	232·5	4·2
Poly ACGU	3·2	258	11·3	230	3·9	260	10·6	231	4·9
Yeast RNA	5·1	259·5	10·2	231·5	3·35	260	9·7	233	5·2
RNAase resistant core	6·2	257	11·1	230	3·5	259	10·5	231	4·4
P5′U Poly A	6·7	257	11·3	231	3·2	258	10·0	229	2·6
P5′U Poly A	4·0	257	13·4	230	3·55	258	11·7	229	2·7
P5′U Poly U	5·4	260	8·8	230	2·2	260	6·4	243	5·2
P5′U Poly U	3·4	260	8·8	230	2·2	260	6·4	242	5·1
Uridine-2′(3′) phosphate	—	262	10·0	230	2·0	261	7·7	242	5·3
Guanosine-2′(3′) phosphate	—	257	12·2	228	2·6	260—265	11·1	230	4·3

* At 260 mμ.

TABLE 4.

	Average chain length	Optical density ratios: In 0·01N-HCl 280/260 mμ	In 0·01N-HCl 250/260 mμ	In 0·01N-NaOH 280/260 mμ	In 0·01N-NaOH 250/260 mμ
P5′U Poly A	6·7	0·28	0·86	0·27	0·61
P5′U Poly A	4·0	0·26	0·86	0·23	0·81
P5′U Poly U	5·4	0·34	0·78	0·26	0·87
P5′U Poly U	3·4	0·32	0·79	0·23	0·87
Poly U	11·9	0·36	0·77	0·29	0·87
Poly U	6·6	0·34	0·77	0·27	0·87
Poly U	3·5	0·32	0·77	0·27	0·87
Poly G	12·5	0·64	0·90	0·61	0·85
Poly G	5·4	0·64	0·90	0·62	0·84
Poly G	3·2	0·65	0·93	0·62	0·86
Adenosine-2′(3′) phosphate	—	0·22	0·85	0·15	0·80
Diadenylic	—	—	—	0·22	0·80
Triadenylic	—	—	—	0·24	0·805
Tetra-adenylic	—	—	—	0·26	0·81
Penta-adenylic	—	—	—	0·285	0·83
Poly A	13·6	0·31	0·90	0·29	0·84
Poly A	7·7	0·28	0·87	0·27	0·82
Poly A	3·3	0·25	0·84	0·25	0·81

decrease in $\epsilon_{max.}$ when equal amounts of polyuridylic and polyadenylic acid (both of chain length ~12 units) were mixed, even when the solution was made 10^{-4}M with respect to magnesium. Lack of macromolecular interaction was confirmed by paper electrophoresis

—the mixture separated into two discrete spots identical with polymer markers, again quite unlike the behaviour of the mixed biosynthetic polymers.[40]

The small hypsochromic shift noted by Warner [40] has also been observed with some of the synthetic polymers, particularly the polyadenylic acids. Variation of optical-density ratios with increase in chain length is shown in Table 4, and Figs. 5 and 6 illustrate the anomalous ultraviolet absorption of adenosine-2′ uridine-5′ phosphate and triadenylic acid compared with the spectra obtained on alkaline degradation.

Polymerisation can also cause pronounced changes in the apparent pK_a values of the bases, particularly with polyguanylic acids. Thus spectrophotometric titrations indicated

FIG. 3. *Polyguanylic acid (average chain length 12·5 units). A, in* 0·01N-HCl; *B, in* 0·01N-NaOH; *C, in* H_2O, pH 7.

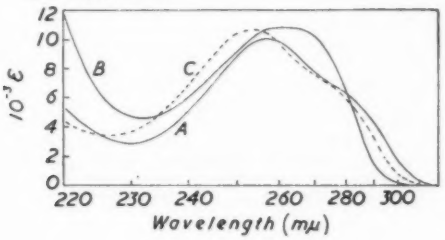


FIG. 4. *Polyuridylic acid (average chain length 12·4 units). A, in* 0·01N-HCl; *B, in* 0·01N-NaOH.

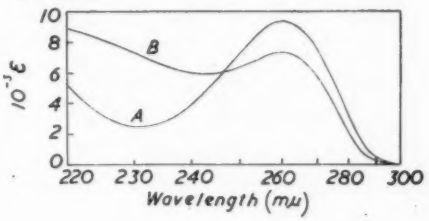


FIG. 5. *Action of alkali on adenosine-2′ uridine-5′ phosphate. A, in* 0·2N-NaOH, *before hydrolysis; B, products.*

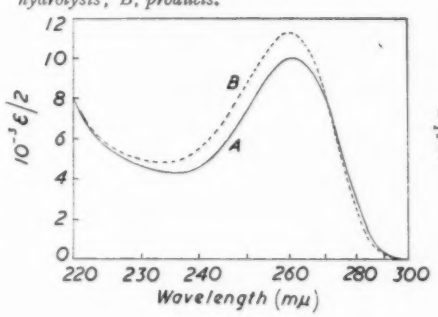
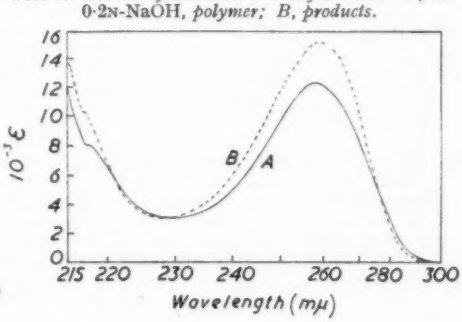


FIG. 6. *Action of alkali on triadenylic acid. A, in* 0·2N-NaOH, *polymer; B, products.*



that the apparent pK of 2·32 for guanosine-2′(or 3′) phosphate was shifted to 2·63 for polyguanylic acid with an average chain length of 5·4 units, while in the alkaline region shifts from 9·33 to 10·76 (for polymer with an average chain length of 5·4 units) and to 11·20 (for polyguanylic acid, average length 12·5 units) were noted (Fig. 7).

If, as seems reasonable, even in the relatively small synthetic polymers, the purine and/or pyrimidine bases are to some extent stacked in layers above each other, interaction of π-electrons of adjacent rings [41] causes essentially a new electronic species with an ultraviolet absorption characteristic of the entire molecule, rather than a simple summation of the independent absorption of the component mononucleotides. This interaction of the π-electron systems, evident in the altered absorption spectrum, would also have an effect on the ionisable groups of the purines and pyrimidines, since they participate directly in the chromophoric systems. Also, perturbation of these groups, by hydrogen bonding or

[41] Laland, Lee, Overend, and Peacocke, *Biochim. Biophys. Acta*, 1954, **14**, 356; Scott, in "Physical Techniques in Biological Research," ed. Oster and Pollister, Academic Press, New York, 1955, Vol. I, p. 144.

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ionisation, would affect the π-electron interaction of the total chromophoric system. Variation in ionic strength or other factors changing the macromolecular configuration and superstructure (*e.g.*, bonding between helices or different parts of a single helix) would likewise affect this basic interaction and hence the absorption. Indeed the influence of the macromolecular superstructure of undenatured nucleic acids seems to account for some 50% of the total hypochromicity, as shown on denaturation by mild acid, alkaline, or heat treatment.[42]

Certain planar basic dyes are bound by nucleic acids; these dyes also fail to obey Beer's law in aqueous solution, owing to molecular aggregation in the more concentrated solutions. The effect of the synthetic polymers on the absorption spectra of dilute solutions of Rosaniline, Toluidine Blue, and Acridine Orange is shown in Figs. 8—10. Equimolar amounts of dye and polymer phosphate were used in order to avoid the inter-

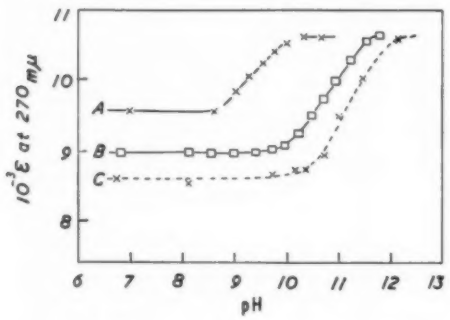


FIG. 7. *Spectrophotometric titration at* 270 mμ *of* (*A*) *guanosine-2′(3′) phosphate,* (*B*) *polyguanylic acid* (*average chain length* 5·4 *units*), *and* (*C*) *polyguanylic acid* (*average chain length* 12·5 *units*).

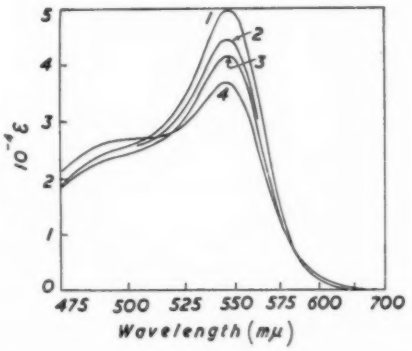


FIG. 8. *Action of polynucleotides* [2×10^{-5}M-(P)] *on the absorption spectrum of Rosaniline* (2×10^{-5}M) *in* 0·01M-*ammonium acetate at* pH 6·8. 1, *Dye alone;* 2, 3, *and* 4, *with added polyuridylic, polyguanylic, and commercial yeast ribonucleic acid respectively.* (All polymers with an average chain length of ~6 units.)

planar reaction between dye and purine ring systems observed between a large excess of adenosine and riboflavin,[43] and to avoid " monomeric " binding [44] to phosphate groups, which would presumably arise if a large excess of polymer were employed. In all cases the effects of the synthetic polymers were smaller than those of yeast ribonucleic acid, possibly because of distortion due to the irregular distribution of 2′–5′-internucleotide linkages in the synthetic materials. Marked quenching of the fluorescence of Acridine Orange was also observed, but again, while comparable with that due to yeast ribonucleic acid, the effect was smaller for the synthetic polymers. The low hypochromicity of polyuridylic acid at neutrality may be compared with its much smaller effects on the various dyes, and with the negligible shift in apparent p*K*. Polyglycerophosphoric acid

[42] Lawley, *Biochim. Biophys. Acta*, 1956, **21**, 481.
[43] Weber, *Biochem. J.*, 1950, **47**, 114.
[44] Lawley, *Biochim. Biophys. Acta*, 1956, **19**, 328.

produced no spectral changes or quenching of fluorescence, indicating that the phosphate binding sites must be suitably spaced to produce metachromasy in combined dyes.

The physical properties show that the synthetic polymers, although relatively small, have configurations involving stacking of purines and/or pyrimidines parallel to each other, in aqueous solution. To some extent, even dinucleotides can be regarded as having only a limited freedom of movement about the internucleotide linkage under normal conditions.

FIG. 9. *Action of polynucleotides* [3×10^{-5}M-(P)] *on the absorption spectra of Acridine Orange* (3×10^{-5}M) (*left*) *and Toluidine Blue* (3×10^{-5}M) (*right*), *in* 0·01M-*ammonium acetate at* pH 6·8. 1, *Dye alone;* 2, 3, 4, *and* 5, *with added polyuridylic, polyadenylic, polyguanylic, and yeast ribonucleic acid respectively.*

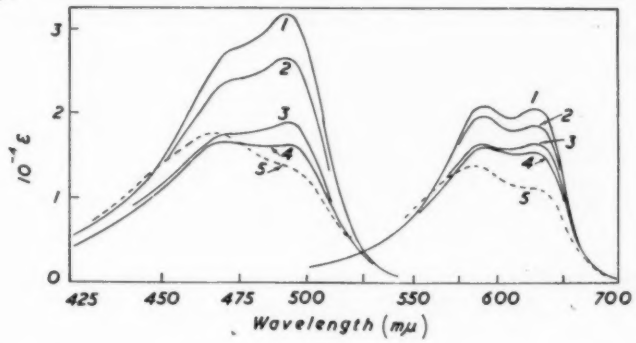
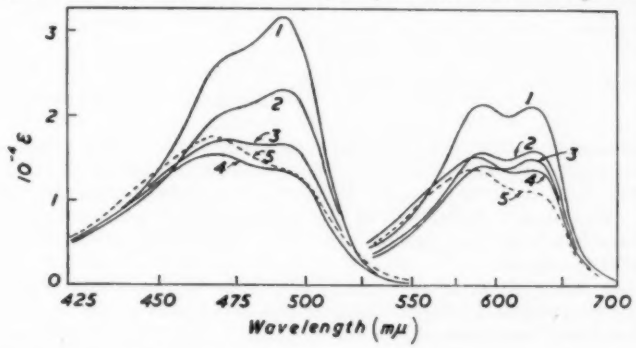


FIG. 10. *Action of polynucleotides* [3×10^{-5}M)-(P)] *on the absorption spectra of Acridine Orange* (3×10^{-5}M) (*left*) *and Toluidine Blue* (3×10^{-5}M) (*right*), *in* 0·01M-*ammonium acetate at* pH 6·8. 1, *Dye alone;* 2, 3, 4, *and* 5, *with added synthetic "ribonucleic acid," polyadenylic-guanylic acid, ribonuclease-resistant "core" material from yeast nucleic acid, and yeast ribonucleic acid respectively.*



Biological Properties of the Polymers.—Dr. M. McCarty of the Rockefeller Institute or Medical Research, New York, has demonstrated an immunochemical relation between natural and synthetic polyglycerophosphoric acid. Precipitation occurred with the synthetic material and antiserum (prepared with heat-killed group A *Streptococci*) selected because of its reactivity with a bacterial substance, identified as natural polyglycerophosphoric acid. Certain other antisera, with which the synthetic material did not give precipitates, showed specific inhibition of the reaction with the bacterial antigen. Drs. D. Shugar and H. Tomerska of the Polish Academy of Sciences, Warsaw, have found that the synthetic polyguanylic acid is highly active (considerably more so than natural nucleic acids) in inducing streptolysin S formation in *Streptococci*, while Drs. G. B. Brown and J. J. Biesele of the Sloan-Kettering Institute for Cancer Research, New York, report that,

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although polyuridylic acid had no action on tissues in culture, polyadenylic acid was an effective inhibitor.

Experimental

Polyglycerophosphoric Acid.—A solution of glycerol 2-(disodium phosphate) (10 g.) in water (250 c.c.) was run through a column of IR-120 resin (H^+ form, 3 × 20 cm.). To the eluate and washings was added tri-*n*-octylamine (15 c.c.), and the mixture evaporated to dryness under reduced pressure, dioxan, ethanol, and toluene being added from time to time. The viscous residue was further dried by evaporation with more dry dioxan and toluene and finally dissolved in dioxan (35 c.c.). Diphenyl phosphorochloridate [2] (8·5 c.c., 1·25 mol.) followed by tri-*n*-butylamine (18·9 c.c., 2·5 mol.) were added, with shaking, under anhydrous conditions and the clear solution was kept at room temperature for 1½ hr. More diphenyl phosphorochloridate (8·5 c.c.) and tri-*n*-butylamine (18·9 c.c.) in dioxan (35 c.c.) were then added and the solution was kept at room temperature for a further 3 hr. After concentration under reduced pressure until a slight turbidity appeared water (30 c.c.) was added, and the mixture left at 0° overnight. Two volumes of ethanol (approx. 250 c.c.) were added, followed by an ethanolic solution of calcium chloride (3·5 g.). After ½ hr. the white precipitate of *calcium polyglycerophosphate* was collected by centrifugation, washed with acetone, then ether, and dried (4·5 g.). A further 2·3 g. were obtained from the mother-liquors by addition of acetone. The crude material was purified by reprecipitation or by dialysis against water [Found, in the dialysate specimen, dried at 90°/10^{-3} mm. for 24 hr.: P, 17·85. Found in dialysis residue: P, 17·9. $(C_3H_6O_5PCa_{\frac{1}{2}})_x$ requires P, 17·9%].

Paper Chromatography.—Ascending chromatograms on Whatman No. 1 paper were used with solvent systems: *A*, ethanol–M-ammonium acetate (5 : 2); *B*, *tert.*-amyl alcohol–formic acid–water (3 : 2 : 1); and *C*, propan-2-ol–ammonia (*d* 0·88)–water (14 : 1 : 5). Results were:

	R_F		
	A	*B*	*C*
β-Glycerophosphate	0·23	0·54	0·26
Glycerol-1 : 2 cyclic phosphate	0·50	—	0·66
Glycerol-1 : 2(3) diphosphate	0·02	0·34	0·02
Polyglycerophosphoric acid	0 to 0·12	0·05 to 0·30	0 to 0·12
Polyglycerophosphoric acid treated with 0·1N-HCl at 100°/2 hr.	0·03 & 0·24	0·37 & 0·56	0 & 0·28
Polyglycerophosphoric acid treated with 0·1N-NaOH at 37°/24 hr.	0·02 & 0·23	0·34 & 0·54	0·05 & 0·24

Action of Ribonuclease.—Calcium polyglycerophosphate (3 mg.) and crystalline ribonuclease (0·3 mg.) were dissolved in water (0·5 c.c.), and the solution adjusted to pH 7·2 with dilute ammonia, and incubated at 37° for 24 hr. Paper chromatography showed that no degradation had occurred. Rattlesnake venom had no action on either β-glycerophosphoric acid or the polymer. Prostate monoesterase had no action on the polymer until the terminal cyclic phosphate had been opened.

Action of Acid on Polyglycerophosphoric Acid to open the Terminal Cyclic Phosphate Group.—Calcium polyglycerophosphate (500 mg.) was left in 0·1N-hydrochloric acid (5 c.c.) at room temperature for 3 hr., then neutralised with 2N-ammonia (0·25 c.c.). Calcium chloride was added followed by ethanol (30 c.c.). The precipitated *calcium salt* was collected by centrifugation, washed with ethanol, then ether, and dried (475 mg.) (Found in material dried at 90°/10^{-3} mm. for 24 hr.: P, 17·65%. Average chain length 6·4 units). Dialysis against 2M-sodium chloride gave a residue (110 mg.) with an average chain length of 12·1 glycerophosphate units.

Determination of Chain Length by Purified Prostate Phosphatase.—Inorganic and total phosphate were estimated after incubation at 37° of solutions of the polymer and of glycerophosphate in 0·05M-ammonium citrate at pH 5, with 0·1 c.c. of a stock solution of purified prostate phosphatase per c.c. of substrate solution. (Phosphatase solution *ca.* 0·5 mg./c.c. Substrate 2 mg./c.c.)

After ½ hr. the β-glycerophosphate was completely dephosphorylated, and liberation of inorganic phosphate from the polymer reached a limit at 12 hr.

Glycerol Monophosphate.—A mixture of glycerol (5 c.c.), phosphoric acid (10 g.), and

phosphoric anhydride (10 g.) was kept at 60° for 1 hr. with exclusion of moisture and occasional stirring. The syrup was then heated in water (100 c.c.), on a water-bath for 30 min. Aqueous lithium hydroxide was added to pH 8·3, and the filtered solution passed through a column of IR-120 (H^+ form) to remove cations. Aqueous barium hydroxide was added to the eluate and water washings, to pH 7·4, and the precipitated barium phosphate removed by centrifugation. The supernatant liquid and washings were concentrated to 300 c.c., and the solution was boiled gently for 5 min. and filtered hot. The filtrate was concentrated to 100 c.c., two volumes of ethanol were added, and the precipitated barium glycerophosphate was collected, washed with ethanol, then acetone, and dried (7·75 g.) (Found, in material dried at 90°/10^{-3} mm. for 12 hr.: P, 10·4. Calc. for $C_3H_7O_6PBa$: P, 10·1%).

Glycerol Diphosphate.—A mixture of glycerol (5 c.c.), phosphoric acid (20 g.), and phosphoric anhydride (25 g.) was kept at 60° for 2 hr., then dissolved in water (100 c.c.) and kept at 100° for 30 min. Aqueous lithium hydroxide was then added to pH 8·3, and the mixture left at 0° overnight, then filtered. The filtrate was concentrated to 100 c.c., excess of barium bromide added, the mixture boiled for 5 min., and the precipitated solid collected from the hot suspension. This crude salt was dissolved in the minimum quantity of 2N-hydrobromic acid and diluted to 50 c.c., and the pH adjusted to 1. Ethanol (3 vols.) was added and the precipitated *glycerol barium hydrogen diphosphate* purified by reprecipitation from the acidic solution with ethanol (10·8 g.) (Found: P, 14·6. Calc. for $C_3H_8O_9P_2Ba,2H_2O$: P, 14·7%).

Uridine Phosphates.—The free acid (1 mol.) was dissolved in methanol, tri-*n*-octylamine (1 mol.) added, and the solution evaporated to dryness. The residual solid foam was dried by evaporation with anhydrous dioxan and toluene and stored over P_2O_5 *in vacuo* at room temperature.

Adenosine and Guanosine Phosphates.—Tri-*n*-decylamine (1 mol.) and the free acid (1 mol.) were boiled in 1 : 1 methanol–ethanol, until dissolution was effected. The solution was then evaporated and dried as above to give a white solid foam.

Uridine-2′ : 3′ Cyclic Phosphate.—(a) *With diphenyl phosphorochloridate.* Uridylic acid(-2′ and -3′) (100 mg.) was converted into the anhydrous monotri-*n*-octylamine salt which was dissolved in anhydrous dioxan (5 c.c.) and benzene (5 c.c.). Diphenyl phosphorochloridate (0·105 g., 1·25 mol.) was then added followed by tri-*n*-butylamine (0·184 c.c., 2·5 mol.), and the clear solution kept at room temperature for 2 hr., with occasional shaking. Solvent was then removed under reduced pressure, and *cyclo*hexane (10 c.c.) added to the residue with shaking. The precipitated gum was dissolved in ethanol (5 c.c.) and neutralised to pH 7·4 with 2 : 6-lutidine, and ethanolic calcium chloride was added. The precipitated calcium salt was centrifuged off, washed with absolute ethanol, then ether, and dried. Reprecipitation by dissolution in a little water and addition of 1 : 1 ethanol–acetone gave the pure *calcium uridine-2′ : 3′-cyclic phosphate* (90 mg.). Paper chromatography of the initial reaction mixture showed that complete reaction occurred, the cyclic phosphate being the sole product, chromatographically identical with an authentic sample [Found, in material dried at 50°/10^{-3} mm. for 12 hr.: N, 8·4; P, 9·4. Calc. for $(C_9H_{10}O_8N_2P)_2Ca$: N, 8·6; P, 9·5%].

(b) *With tetraphenyl pyrophosphate.* Tri-*n*-octylammonium uridine-2′(3′) phosphate (from 50 mg. of the nucleotide) in dioxan (2 c.c.) was added to tetraphenyl pyrophosphate [3] (94 mg., 1·25 mol.), followed by tri-*n*-butylamine (0·092 c.c., 2·5 mol.), and the clear solution was left at room temperature for 2 hr. Paper chromatography showed complete conversion into the cyclic phosphate. Ethanolic calcium chloride was added, and the precipitated calcium salt purified as described above (yield 95%).

Adenosine-2′ : 3′ Cyclic Phosphate.—Yeast adenylic acid (200 mg.) as the anhydrous tri-*n*-decylamine salt was dissolved in anhydrous dioxan (15 c.c.) and to the solution, stirred under anhydrous conditions, was added diphenyl phosphorochloridate (0·195 g., 1·25 mol.) in benzene (1 c.c.). The solution was kept at room temperature for 2 hr., then evaporated under reduced pressure, the residue shaken with *cyclo*hexane (20 c.c.), and the precipitated gum dissolved in ethanol (10 c.c.), neutralised to pH 7·5 with 2 : 6-lutidine, and treated with ethanolic calcium chloride. The precipitated calcium salt was centrifuged off and purified in the usual manner. (200 mg.) [Found, in material dried at 50°/10^{-3} mm. for 12 hr: N, 19·9; P, 9·2. Calc. for $(C_{10}H_{11}O_6N_5P)_2Ca$: N, 20·1; P, 8·9%]. Tetraphenyl pyrophosphate gave similar results.

Polyadenylic Acid.—Diphenyl phosphorochloridate (0·65 c.c.) and tri-*n*-butylamine (1·25 c.c.) were added to a solution of mono(tri-*n*-decylammonium) adenosine-2′ : 3′ cyclic phosphate

[from 0·75 g. of adenosine-2′(3′) phosphate] in dioxan (10 c.c.) with stirring under anhydrous conditions. After 3 hr. at room temperature, solvent was removed under reduced pressure, and ether (50 c.c.) added to the residue with shaking. The precipitate was collected, washed with ether, and dried. The crude material was dissolved in water (10 c.c.), ammonia was added to pH 8·0, then ethanol and 2N-hydrochloric acid to precipitate the polyadenylic acid which was centrifuged off, washed with ethanol, then ether, and dried (0·72 g.).

A similar yield was obtained when the diphenyl phosphorochloridate was replaced by an equivalent amount of tetraphenyl pyrophosphate.

Polyuridylic Acid.—Mono(tri-*n*-octylammonium) uridine-2′(3′) phosphate (from 0·75 g. of the nucleotide) in dioxan (10 c.c.) was treated with diphenyl phosphorochloridate (0·70 c.c.) and tri-*n*-butylamine (1·40 c.c.) to prepare the cyclic phosphate. Further quantities of diphenyl phosphorochloridate (0·70 c.c.) and tri-*n*-butylamine (1·40 c.c.) were added and the solution was kept at room temperature for 3 hr. Solvent was removed under reduced pressure, ether (50 c.c.) added to the residue, and the precipitated material dissolved in water (10 c.c.), the pH being adjusted to 8·7 with ammonia. The solution was extracted twice with ether to remove amines, and the polyuridylic acid was isolated as the calcium salt (0·73 g.) by the addition of calcium chloride and ethanol. Alternatively the polymer was obtained as the magnesium salt by the addition of ethanolic magnesium chloride.

A similar run from uridine-2′(3′) phosphate (100 mg.), as the mono(tri-*n*-octylammonium) salt in dioxan (1 c.c.), and tetraphenyl pyrophosphate (376 mg.) and tri-*n*-butylamine (0·37 c.c.) gave a 100% yield of polymer.

Polyguanylic Acid.—An aqueous solution of disodium guanosine-2′(3′) phosphate (0·5 g.) was run through a small column of IR-120 (H^+ form), and to the eluate and water washings was added tri-*n*-decylamine (0·7 c.c., 1 mol.). The mixture was evaporated to dryness with ethanol, dioxan, and dimethylformamide under reduced pressure to give the anhydrous salt. This was dissolved in dioxan (4 c.c.), diphenyl phosphorochloridate (0·45 c.c.) and tri-*n*-butylamine (0·9 c.c.) were added with shaking under anhydrous conditions, and the mixture was shaken for a further 2 hr. at room temperature. To the solution of guanosine-2′ : 3′ cyclic phosphate were added more diphenyl phosphorochloridate (0·5 c.c.) and tri-*n*-butylamine (0·9 c.c.), and the mixture was evaporated to *ca.* 5 c.c. under reduced pressure, and kept at room temperature for 3 hr., then worked up in the usual way after precipitation of the crude product with a mixture of ether (15 c.c.) and *cyclo*hexane (15 c.c.), final washing being with ether. The crude product (0·4 g.) was purified by the addition of ethanol containing hydrochloric acid to a solution of the ammonium salt (250 mg.). A similar run from 3 g. of sodium guanylate yielded 1·5 g. of polymer.

Polyadenylic-cytidylic-guanylic-uridylic Acid.—Tri-*n*-octylamine (0·144 c.c.) was added to a mixture of uridine-2′(3′) phosphate (20 mg.), adenosine-2(3′) phosphate (35 mg.), guanosine-2(3′) phosphate (15 mg.), and cytidine-2(3′) phosphate (30 mg.) in aqueous ethanol, and the solution evaporated to dryness. The residue was dissolved in ethanol and re-evaporated to dryness under reduced pressure and finally dried by repeated evaporation to dryness of the dioxan solution, giving a solid foam. This was dissolved in dioxan (1 c.c.). Diphenyl phosphorochloridate (0·09 c.c.) and tri-*n*-butylamine (0·19 c.c.) were added and the mixture was shaken under anhydrous conditions for 1 hr. Fresh diphenyl phosphorochloridate (0·09 c.c.) and tri-*n*-butylamine (0·19 c.c.) were then added and the mixture was kept at room temperature for 4 hr. *cyclo*Hexane (10 c.c.) and ether (10 c.c.) were added with shaking, the precipitated material was washed with ether, dried, and dissolved in water (5 c.c.) with the addition of ammonia to pH 8·5, and the solution extracted twice with ether. Acetic acid was added to the aqueous layer to pH 3·5 and the solution kept at room temperature for 48 hr. in order to remove diphenyl phosphate residues from the cytidine amino-groups. Ethanol (15 c.c.) containing 2N-hydrochloric acid (0·2 c.c.) was then added and the white precipitate centrifuged off, washed with ethanol and ether, and dried (58 mg.).

The supernatant liquids yielded a further 35 mg. of calcium polynucleotide on treatment in the usual way.

A similar run from a mixture of the cyclic phosphates from 250 mg. of each nucleotide and diphenyl phosphorochloridate (1·0 c.c.) and tri-*n*-butylamine (1·8 c.c.) yielded 0·6 g. of copolymer, the dialysis residue of which had a molar ratio of adenine 3·67, guanine 2·17, uracil 2·42, and cytosine 1·0. The dialysate had adenine 2·3, guanine 1·7, uracil 1·3, and cytosine 1·0.

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Polyadenylic-guanylic Acid.—A mixture of the mono(tri-*n*-decylammonium) salts of adenosine-2′(3′) phosphate (0·5 g. of the free acid) and guanosine-2′(3′) phosphate (from 0·5 g. of the disodium salt) in anhydrous dioxan (10 c.c.) was treated in the usual way with diphenyl phosphorochloridate (0·9 c.c.) and tri-*n*-butylamine (1·8 c.c.) to give the cyclic phosphates. Addition of the same quantity of reagents and reaction for 4 hr. at room temperature gave the mixed polymer which was isolated as the free acid (600 mg.). Dialysis against water gave a dialysis residue (380 mg.) which had a molar ratio adenine 2, guanine 1.

Polymers containing Various Proportions of Uridylic and Adenylic Acids.—These were prepared in the usual way from various ratios of uridylic and adenylic acid. Acid precipitation gave polymers richer in adenylic acid than the starting ratio when a large excess of adenylic acid was not used, owing to the greater solubility of polymers containing more uridylic than adenylic acid.

Poly AU (1 : 2).—To a solution of uridine-2′(3′) phosphate (200 mg.) and adenosine-2′(3′) phosphate (100 mg.) as the mono(tri-*n*-octylammonium) salt and mono(tri-*n*-decylammonium) salt respectively in dioxan (5 c.c.) were added tetraphenyl pyrophosphate (1·11 g. 2·5 mol.) and tri-*n*-butylamine (1·08 c.c., 5 mol.), and the solution was then evaporated to *ca.* 3 c.c. under reduced pressure and left at room temperature for 3 hr. A 1 : 1 mixture (10 c.c.) of ether and *cyclo*hexane was added, and the precipitate centrifuged off, washed with ether, and dried. The crude material was dissolved in water (4 c.c.), neutralised with aqueous ammonia, and extracted twice with ether. Three volumes of ethanol were added, followed dropwise by 2N-hydrochloric acid until precipitation was complete. The precipitate was centrifuged off, washed with alcohol, then ether, and dried (180 mg.). Degradation showed that the molar ratio of this material was adenine 1, uracil 1·25.

Polyadenylic-uridylic Acid (*Tracts*).—Adenosine-2′(3′) phosphate (250 mg.) and uridine-2′(3′) phosphate (250 mg.) were each separately converted into polymers of low molecular weight in dioxan (20 c.c.) as previously described. After 2 hr. at room temperature (paper chromatography showed largely di-, tri-, and tetra-nucleotides) the two solutions were combined and evaporated under reduced pressure to *ca.* 10 c.c. A further quantity of diphenyl phosphorochloridate (0·3 c.c.) and tri-*n*-butylamine (0·6 c.c.) was added with shaking, and the mixture kept at room temperature for 3 hr. Solvent was then removed under reduced pressure, and *cyclo*hexane (50 c.c.) added to the residue with shaking. The precipitate was washed with ether (25 c.c.) and dissolved in water (5—10 c.c.), 2 : 6-lutidine being added to neutrality. After extraction with ether, ethanol and 2N-hydrochloric acid were added to the aqueous layer to precipitate the polymer, which was washed with alcohol, acetone, and ether, and dried (385 mg.).

The mother-liquors were neutralised with 2 : 6-lutidine and alcoholic calcium chloride was added. The calcium salts were centrifuged off, washed with alcohol, then ether, and dried (145 mg.).

Dialysis of Polymers.—A neutral solution of each polymer (*ca.* 2 mg.) in water (2 c.c.) was dialysed in Visking tubing against two changes of water (20 c.c.), then against two changes of 2M-sodium chloride (20 c.c.) for 24 hr. each. The final dialysis residue was then diluted to 40 c.c., and the absorption of each fraction measured at 260 mμ. The results are expressed as a percentage of the total absorption. Because of the increase in hypochromicity of polynucleotides with molecular size, the actual weight percentages would be somewhat larger for the dialysis residues. It should also be emphasised that the results refer to the crude products representing a quantitative yield, before fractionation. Determination of chain length indicated that dialysis against water left a residue with an average chain length of 5—6 units. Dialysis against 2M-sodium chloride gave a residue of average chain length 10—12 mononucleotides:

	Dialysate		
	Water	2M-NaCl	Residue
Poly U	31·8	45·7	22·5%
Poly A	24·9	45·5	29·6%
Poly G	15·8	38·0	46·2%
P5′U Poly A	19·9	46·6	33·5%
Poly AU (1·42 : 1)	19·8	46·6	33·6%
Poly AU (4·54 : 1)	20·7	47·0	32·3%
Poly ACGU	18·5	43·3	38·2%
Yeast RNA	14·8	29·8	55·4%

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Dialysis of concentrated solutions of the polymers against three changes of 5—10 volumes of water on a preparative basis gave the following yields (g.), slight losses occurring during the isolation:

Compound	Amount	Dialysate	Dialysis residue
Calcium polyuridylate	0·90	0·29	0·575
Polyadenosine-2′(3′) phosphate	0·90	0·34	0·515
Polyguanosine-2′(3′) phosphate	1·75	0·405	1·18
Calcium 5′-phosphouridine-2′(3′) phosphopolyuridylate	0·50	0·205	0·265
5′-Phosphouridine-2′(3′) phosphopolyadenosine-2′(3′) phosphate	0·65	0·24	0·37
Polyadenylicguanylic acid	0·60	0·20	0·38
Poly ACGU	0·50	0·185	0·28
5′-(Benzyl phosphite) polyadenosine-2′(3′) phosphate	0·90	0·46	0·15
Calcium polyglycerophosphate	5·00	1·70	2·64

Purification of Commercial Yeast Ribonucleic Acid.—The nucleic acid (10 g.) was dissolved in water with the addition of 2N-ammonia to pH 7·8, and the solution placed in Visking tubing and dialysed against five volumes of water for 24 hr. This process was repeated three times and the dialysis residue treated with 2N-hydrochloric acid and ethanol to precipitate the purified nucleic acid which was collected, washed with ethanol and ether, and dried (5·8 g.). From the concentrated combined dialysates, a similar procedure gave 2·7 g. of material. Hydrolysis to mononucleotides, and separation and estimation by the usual methods, gave the following molar ratios for the purified nucleic acid; adenine 1·0, guanine 0·98, cytosine 0·80, uracil 1·0; average chain length 5·2.

Ribonuclease-resistant Cores from Yeast Nucleic Acid.—To an aqueous solution of nucleic acid (10 g. in 300 c.c.) at pH 8 with ammonia, was added ribonuclease (10 mg.), and the solution was incubated at 37° for 48 hr., dilute ammonia being added occasionally to maintain pH 7·2. A further quantity of ribonuclease (5 mg.) was added after 24 hr. The solution was then dialysed against several changes of water, and the ribonuclease-resistant cores were precipitated by 2N-hydrochloric acid and ethanol, collected by centrifugation, washed with ethanol, then ether, and dried (2·4 g.). Estimation by the usual methods gave an average chain length of 6·1 units and molar ratios of adenine 1·0, guanine 1·15, cytosine 0·20, uracil 0·23.

Adenylic-cytidylic dinucleotide (A3′P5′C3′P) was isolated from the dialysates obtained as above, by ion-exchange chromatography on Dowex 1 × 2. Recrystallisation from water gave needles, m. p. 212° (decomp.) (Found, in material dried at 90°/10^{-3} mm.: N, 17·2; P, 9·6. $C_{19}H_{26}O_{14}N_8P_2$ requires N, 17·2; P, 9·5%).

Adenosine-2′ Uridine-5′ Phosphate.—Prepared as previously described,[45] the crystalline material had $\lambda_{max.}$ 261 mμ (ε 21,600), $\lambda_{min.}$ 231 mμ (ε 4600) in water at pH 7.

Viscosity.—An average of 10 readings of 1% solutions of the sodium salts in an Ostwald viscometer gave the following results: water 76·8 sec.; yeast ribonucleic acid 79·6 sec., polyadenylic acid 79·3 sec.

Action of Alkali on Polymers.—Treatment with 0·2N-sodium hydroxide at 37° for 24 hr. gave the expected nucleotides or mixtures of nucleotides, separated by paper chromatography and paper electrophoresis.

Action of Acid on Polymers.—Treatment of polyuridylic acid with 0·1N-hydrochloric acid at 37° for 48 hr. caused hydrolysis to the mixed 2′- and 3′-mononucleotides. The polypurine nucleotides were broken down to purines by the action of N-hydrochloric acid at 100°.

Action of Rattlesnake Venom on Polymers.—To the substrate (approx. 2½ mg.) in glycine buffer (0·3 c.c. of 0·25M-solution at pH 9·0) were added 0·1M-magnesium chloride (0·1 c.c.) and rattlesnake (*Crotalus atrox*) venom (0·2 c.c. of a solution of 20 mg. of venom in 1 c.c. of 0·1M-potassium chloride), and the mixture was incubated at 37° for 2 days. Paper electrophoresis on Whatman No. 1 paper in 0·02M-disodium hydrogen phosphate at 10 v/cm. for 1 hr. separated the nucleoside (adenosine and uridine were also separated in this system) and nucleoside-2′(3′) : 5′ diphosphate which were eluted with 0·1N-hydrochloric acid and estimated spectroscopically to give the average chain length. Alternatively paper chromatography in ethanol–M-ammonium acetate (5 : 2) was used for the separation.

[45] Michelson, Szabo, and Todd, *J.*, 1956, 1546.

The crude venom seemed to be somewhat more active against polyuridylic acid than against polyadenylic or polyguanylic acid.

Estimation of Chain Lengths by using Purified Prostate Monoesterase.—Stock monoesterase (0·8 c.c. of an aqueous solution containing 1 mg./c.c.) was added to a solution of the substrate (16 mg.) in 0·05M-citrate buffer at pH 5 (8 c.c.), and the mixture incubated at 37°. Aliquot parts were removed at timed intervals, and total and inorganic phosphate were estimated by Allen's method.[46] For polyuridylic and polyguanylic acid, the procedure was modified so as to include a preliminary acid treatment to open the terminal cyclic phosphate. To a solution of calcium polyuridylate (16 mg.) in water (2 c.c.) was added 0·2N-hydrochloric acid (2 c.c.), and the solution kept at room temperature for 3 hr. Then 2N-sodium hydroxide (0·2 c.c.) was added, followed by 0·1M-citrate at pH 5 (4 c.c.) and stock phosphatase solution (0·8 c.c.), and the solution was incubated as above. Dephosphorylation of the terminal phosphate was complete in 6—12 hr.

Action of Ribonuclease on Polyuridylic Acid.—Ribonuclease (1·8 mg.) was added to a solution of calcium polyuridylate (250 mg.) in water (10 c.c.), and the whole was adjusted to pH 7·4 with aqueous ammonia and kept at 37° for 24 hr., 0·2N-ammonia being added to keep the pH between 7·1 and 7·4. Ethanolic calcium chloride (100 mg.) was then added, followed by ethanol (40 c.c.), and the precipitated calcium salt was centrifuged off, washed with alcohol and ether, and dried (250 mg.). A portion of this material was chromatographed on Whatman No. 1 paper (descending) with *tert.*-amyl alcohol–formic acid–water (3 : 2 : 1) as solvent; the bands of uridylic acid, U2′P5′UP, U2′P5′U2′P5′UP, U2′P5′U2′P5′U2′P5′UP, etc., were cut out, eluted with 0·1N-hydrochloric acid, and estimated spectroscopically: mononucleotide 49%, dinucleotide 27%, trinucleotide 12·5%, tetranucleotide 7%, higher polymers 4·5%. This indicates about 65% of 3′–5′- and 35% of 2′–5′-internucleotide linkages. Another specimen gave some 60% of uridylic acid.

Polyadenylic and polyguanylic acid were unaffected by ribonuclease. Mixed purine–pyrimidine polymers were broken down only slightly, owing to the variety of enzyme-resistant linkages.

Polyadenylic Acids of Low Molecular Weight.—Adenosine-2′(3′) phosphate (250 mg.) was converted into the cyclic phosphate in dioxan (20 c.c.) in the usual way. Further quantities of diphenyl phosphorochloridate (0·2 c.c.) and tri-*n*-butylamine (0·4 c.c.) were added with shaking; the clear solution was kept at room temperature for 2 hr., then poured into *cyclo*hexane (75 c.c.), and the precipitated material centrifuged off, washed three times with ether, and dried (230 mg.; average chain length 3·6).

Polyuridylic Acids of Low Molecular Weight.—A solution of uridine-2′(3′) phosphate (250 mg.) as its mono(tri-*n*-octylammonium) salt in dioxan (20 c.c.) was converted into the cyclic phosphate by diphenyl phosphorochloridate (0·21 c.c.) and tri-*n*-butylamine (0·45 c.c., 2·5 mol.) at room temperature for 1 hr. Fresh diphenyl phosphorochloridate (0·21 c.c.) and tri-*n*-butylamine (0·45 c.c.) were then added. After 2 hr. at room temperature the clear solution was poured into *cyclo*hexane (75 c.c.), and the oily precipitate dissolved in 80% ethanol, 2 : 6-lutidine being added to neutrality. An ethanolic solution of calcium chloride (200 mg.) was then added and the calcium salt was centrifuged off, washed with ethanol, then ether, and dried (260 mg.; average chain length 3·3).

Opening of Terminal Cyclic Phosphates.—(A) *Polyuridylic acids of low molecular weight.* The calcium salts (100 mg.) were dissolved in 0·1N-hydrochloric acid (5 c.c.) and kept at room temperature for 4 hr. and the solution was then neutralised with 2 : 6-lutidine. Calcium chloride (100 mg.) in ethanol (20 c.c.) was then added, and the precipitated calcium salt collected by centrifugation, washed with ethanol, then ether, and dried (100 mg.).

(B) *Polyadenylic acids of low molecular weight.* The polyadenylic acids (100 mg.) were dissolved in water (5 c.c.) with the addition of ammonia. 0·2N-Hydrochloric acid (5 c.c.) was then added, and the solution kept at room temperature for 4 hr. (some material was precipitated). After neutralisation of the solution with 2 : 6-lutidine to pH 7·5, magnesium chloride (100 mg.) in ethanol (30 c.c.) was added, and the precipitated magnesium salt collected, washed with ethanol, then ether, and dried (120 mg.).

Separation of Polymers of Low Molecular Weight.—Acid-treated polyadenylic, polyuridylic acid of low molecular weight, and ribonuclease-treated polyuridylic acid were run on Whatman

[46] Allen, *Biochem. J.*, 1940, **34**, 858.

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No. 1 paper (descending) with *tert.*-amyl alcohol–formic acid–water (3 : 2 : 1) as solvent. Appropriate zones were eluted with water, and the eluates neutralised with ammonia and concentrated to small volume under reduced pressure.

Treatment with Purified Prostate Monoesterase.—Samples were treated at 37° for 3 hr. with the monoesterase at pH 5 in 0·05M-ammonium citrate. The uridylic acids lost the terminal phosphate group rather more slowly, as shown by paper chromatography at 1½ hr.

Stability of P¹-*Nucleoside*-5′ P²P²-*Diphenyl Pyrophosphates.*—Treatment of uridine-5′ phosphate and uridine-2′(3′) : 5′ diphosphate with tetraphenyl pyrophosphate gave *P*¹-uridine-5′ *P*²*P*²-diphenyl pyrophosphate and *P*¹-uridine 2′ : 3′-(cyclic phosphate) 5′-*P*²*P*²-(diphenyl pyrophosphate) quantitatively. These were hydrolysed to the corresponding phosphates with 0·1N-hydrochloric acid at room temperature. Instability to alkali was even more marked. Incubation at 37° at pH 9—10 caused complete break-down to uridine-5′ phosphate and uridine-2′(3′) : 5′ diphosphate respectively, within 48 hr.

5′-*Phosphouridine*-2′(3′) *Phosphopolyuridine*-2′(3′) *Phosphate.*—Diphenyl phosphorochloridate (0·5 c.c.) and tri-*n*-butylamine (1·00 c.c.) were added to a solution of mono(tri-*n*-octylammonium) uridine-2′(3′) phosphate (from 0·5 g. of the nucleotide) and bis(tri-*n*-octylammonium) uridine-2′(3′) : 5′ diphosphate (from 0·25 g. of the dibarium salt) in dioxan (7 c.c.), and the solution was kept at room temperature under anhydrous conditions for 1 hr. More diphenyl phosphorochloridate (0·5 c.c.) and tri-*n*-butylamine (1 c.c.) were added and after 3 hr. at room temperature the mixture was worked up as for polyuridylic acid, to give the calcium salt (0·5 g.).

5′-*Phosphouridine*-2′(3′) *Phosphopolyadenosine*-2′(3′) *Phosphate.*—This was prepared as described above, from adenosine-2′(3′) phosphate (0·5 g.) instead of uridine-2′(3′) phosphate, and with working up as for polyadenylic acid (0·5 g.). In each case an aqueous solution of the polymer was adjusted to pH 9—9·5 and kept at 37° for 24 hr. to convert the terminal *P*′-uridine-5′ *P*²*P*²-diphenyl pyrophosphate into a uridine-5′ phosphate unit.

Uridine-2′(3′) *Benzyl Phosphate.*—A solution of uridine-2′(3′) phosphate (0·25 g.) as the tri-*n*-octylamine salt, in dioxan (3·3 c.c.), was treated with diphenyl phosphorochloridate (0·21 c.c.) and tri-*n*-butylamine (0·45 c.c.) to convert it into uridine-2′ : 3′ cyclic phosphate. Benzyl alcohol (0·25 c.c.) followed by diphenyl phosphorochloridate (0·21 c.c.) and tri-*n*-butylamine (0·45 c.c.) were then added, and the solution was kept at room temperature overnight under anhydrous conditions. The crude benzyl esters were worked up as usual and isolated as the barium salts. In addition to a trace of uridylic acid, the product, largely uridine-2′(3′) benzyl phosphate, also contained a compound which was probably a benzyl dinucleotide. The crude product (50 mg.) was separated on a sheet of Whatman No. 1 paper, and the appropriate fraction of uridine-2′(3′) benzyl phosphate eluted with water. The action of ribonuclease (control: RNAase on uridine-2′ : 3′ cyclic phosphate), followed by separation on paper and ultraviolet estimation, showed that ~74% was uridine-3′ benzyl phosphate, the remainder being uridine-2′ benzyl phosphate unaffected even by prolonged treatment (24 hr.) with ribonuclease at 37°.

Paper Chromatography.—R_P values are as follows for ascending chromatograms on Whatman No. 1 paper, the solvent being ethanol–M-ammonium acetate (5 : 2): Uridine-2′(3′) phosphate 0·15; uridine-2′3′ cyclic phosphate 0·47; uridine-2′(3′) benzyl phosphate 0·71; U2′(3′)P5′U2′(3′) benzyl phosphate 0·47; RNAase-treated uridine-2′ : 3′ cyclic phosphate 0·15; RNAase-treated uridine-2′(3′) benzyl phosphate 0·15 and 0·71.

Uridine-2′(3′) *Thymidine*-5′ *Phosphate.*—A solution of uridine-2′ : 3′ cyclic phosphate [from 250 mg. of uridine-2′(3′) phosphate] in dioxan (3·3 c.c.) was added to 3′-*O*-acetylthymidine (0·25 g. anhyd.) in dioxan (3 c.c.), followed by diphenyl phosphorochloridate (0·21 c.c., 1·25 mol.) and tri-*n*-butylamine (0·45 c.c., 2·5 mol.), and the clear solution was left at room temperature overnight. Solvent was removed under reduced pressure, and the residue shaken successively with *cyclo*hexane (10 c.c.) and ether (10 c.c.). The residue was then dissolved in 50% ethanol (20 c.c.), lithium hydroxide was added to pH 9·6, and the solution kept at this pH and at room temperature for 3 days; paper chromatography then showed that deacetylation was complete. Acetic acid was added to pH 8·4, ethanol removed under reduced pressure, and the aqueous solution diluted and run through Dowex 2 × 8 (Cl^- form; 7 × 1·5 cm.) which was washed with water. The aqueous forerun contained the excess of thymidine and was discarded. The column was eluted with 0·01N-hydrochloric acid to remove uridylic acid and uridine-2′(3′) thymidine-5′ phosphate. After neutralisation of the appropriate fractions with ammonia

these were concentrated and further fractionated on sheets of Whatman No. 1 with ethanol–M-ammonium acetate as solvent (descending). The yield of dinucleoside phosphate was low.

Adenosine-2′(3′) Thymidine-5′ Phosphate.—A mixture of adenosine-2′ : 3′ cyclic phosphate (from 250 mg. of adenylic acid) and 3′-*O*-acetylthymidine (250 mg.) in dioxan (10 c.c.) was treated with diphenyl phosphorochloridate (0·2 c.c.) and tri-*n*-butylamine (0·4 c.c.), and worked up as for uridine-2′(3′) thymidine-5′ phosphate.

Paper chromatograms marked for ultraviolet absorbing spots and developed with the cysteine spray [28] showed a series of derivatives APT, APAPT, APAPAPT, etc. A portion of the crude solution was therefore run on sheets of Whatman No. 1 (descending) with ethanol–M-ammonium acetate (5 : 2) as solvent, and appropriate zones were cut out and eluted.

Rechromatography of each zone in *tert.*-amyl alcohol–formic acid–water (3 : 2 : 1), to remove contamination with polyadenylic acids, gave a series of samples which on hydrolysis with 0·2N-sodium hydroxide followed by chromatography (to separate the adenylic acid and thymidine, estimated in the usual way) were shown to be APT, APAPT, APAPAPT, APAPAPAPT.

Polyadenylic Acids with a Terminal 5′-(Benzyl Phosphite) Group.—Diphenyl phosphorochloridate (0·8 c.c.) was added to a solution of mono(tri-*n*-decylammonium) adenosine-2′(3′) phosphate (from 1 g. of the nucleotide) in dry dioxan (20 c.c.), and the solution was left at room temperature for 1 hr., then evaporated to half volume under reduced pressure. *O*-Benzyl-phosphorous *OO*-diphenylphosphoric anhydride (from 1·5 g. of benzyl hydrogen phosphite) in dioxan (10 c.c.) was then added, followed by 2 : 6-lutidine (1 c.c.) with stirring. The solution was set aside at room temperature overnight. Solvent was removed under reduced pressure, and ether (50 c.c.) added to the residue with shaking. The precipitated solid was dissolved in a little dioxan, and tri-*n*-butylamine added to neutrality. Methyl cyanide (25 c.c.) was next added and the precipitated polymer centrifuged off, washed with methyl cyanide and ether, and dried (0·5 g.) (Found, in dialysis residue, isolated in the usual way as the free acid and dried at 40°/10^{-3} mm. for 12 hr.; N, 15·9; P, 11·7. Found, after drying at 80°/10^{-3} mm. for 12 hr.: N, 16·6; P, 12·0%).

5′-Methanesulphonyluridine-2′(3′) Phosphate.—To a solution of uridine-2′ : 3′ cyclic phosphate (from 0·25 g. of uridylic acid) in dioxan (3·3 c.c.) was added methanesulphonyl chloride (0·1 c.c., 1·5 mol.) followed by tri-*n*-butylamine (0·4 c.c.), and the clear solution was left overnight at room temperature. Solvent was then removed under reduced pressure, and *cyclo*hexane (10 c.c.) added to the residue. The precipitated oil was shaken with ether (10 c.c.), the residue dissolved in 0·3N-lithium hydroxide (15 c.c.), and the solution extracted three times with ether, the extracts being discarded. The aqueous layer was kept at room temperature overnight, then neutralised with hydrochloric acid and evaporated to dryness under reduced pressure. The residue was dissolved in 80% ethanol (20 c.c.), and ethanolic calcium chloride added. The precipitated *5′-methanesulphonyluridine-2′(3′) calcium phosphate* was collected by centrifugation, washed with alcohol, then ether, and dried (290 mg.) (Found, in material dried at 90°/10^{-3} mm. for 24 hr: N, 6·2; P, 6·8. $C_{10}H_{13}O_{11}N_2PSCa$ requires N, 6·4; P, 7·0%); in 0·05N-HCl: $\lambda_{max.}$ 261 mμ, $\lambda_{min.}$ 230 mμ, density ratios 280/260 mμ 0·31; 250/260 mμ 0·77; in 0·05N-NaOH; $\lambda_{max.}$ 261 mμ; $\lambda_{min.}$ 240 mμ; density ratios 280/260 mμ 0·29; 250/260 mμ 0·81.

Action of Methanesulphonyl Chloride on Adenosine-2′ : 3′ Cyclic Phosphate.—Mono(tri-*n*-decylammonium) adenosine-2′(3′) phosphate (from 250 mg. of the nucleotide) was converted into the cyclic phosphate in the usual way, in dioxan (10 c.c.). Methanesulphonyl chloride (0·1 c.c., 2 mol.) and tri-*n*-butylamine (0·5 c.c.) were then added and the clear solution was left at room temperature for 6 hr., then at 0° overnight. Solvent was removed under reduced pressure, ether (10 c.c.) added, and the precipitated material collected by centrifugation, washed with ether, dried, then dissolved in dioxan (20 c.c.) with tri-*n*-butylamine to neutrality. The clear solution was heated at 100° for 2 hr. and, after cooling, the precipitated *cycloadenosine-2′ : 3′ cyclic phosphate* was collected, washed and dried (160 mg.) (Found: N, 17·1; P, 7·5. $C_{10}H_{10}O_5N_5P,5H_2O$ requires N, 17·4; P, 7·7%). Light absorption in EtOH: $\lambda_{max.}$ 272 mμ, $\lambda_{min.}$ 236 mμ; density ratios 280/260 mμ 1·17; 250/260 mμ 0·58.

Paper Chromatography.—Ascending chromatograms on Whatman No. 1 paper were used with solvents *A*, *B*, and *C*. Results are tabulated.

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	A	*B*	*C*
Adenosine-2′(3′) phosphate	0·12	0·41	0·25
Adenosine-2′ : 3′ cyclic phosphate	0·42	0·44	0·59
5′-Methanesulphonyladenosine-2′ : 3′ cyclic phosphate	0·52	0·45	0·63
*cyclo*Adenosine-2′ : 3′ cyclic phosphate	0·28	0·38	0·31
Uridine-2′(3′) phosphate	0·18	0·44	0·25
Uridine-2′ : 3′ cyclic phosphate	0·51	0·43	0·51
5′-Methanesulphonyluridine-2′ : 3′ cyclic phosphate	0·58	0·48	—
5′-Methanesulphonyluridine-2′(3′) phosphate	0·22	0·48	0·25
Adenosine	0·60	0·63	—
Uridine	0·71	0·67	0·49
Guanosine-2′(3′) phosphate	0·07	0·33	—
Guanosine-2′ : 3′ cyclic phosphate	0·47	—	—
Cytidine-2′(3′) phosphate	0·11	0·41	—
Cytidine-2′ : 3′ cyclic phosphate	0·54	—	—
APAP	0·04	0·22	—
APAPAP	0·01	0·12	—
APAPAPAP	0	0·04	—
APAPAPAPAP	0	0·01	—
UPUP	0·09	0·24	—
UPUPUP	0·03	0·14	—
UPUPUPUP	0·01	0·04	—
UPUPUPUPUP	0	0·01	—
Uridine-2′(3′) : 5′ diphosphate	—	0·27	—

		A	*B*	*C*
APA		0·22	0·27	—
APAPA		0·07	0·14	—
APAPAPA		0·02	0·07	—
APAPAPAPA		0·0	0·04	—
UPU		0·34	0·36	—
UPUPU		0·16	0·21	—
UPUPUPU		0·07	0·11	—
UPUPUPUPU		0·02	0·05	—
All polymers	2M-NaCl dialysis residue	0·0	0·0	0
	H_2O dialysis residue	0·0	0·0—	0
	H_2O dialysate	—	0·13	—
		—	0 to 0·20	—
Thymidine		0·85	0·73	—
U2′(3′)P5′T		0·52	0·49	—
A2′P5′U		0·30	0·30	—
A2′(3′)P5′T		0·46	0·44	—
APAPT		0·16	0·24	—
APAPAPT		0·05	0·15	—
APAPAPAPT		0·02	0·08	—

Paper Electrophoresis.—Movement towards the anode is tabulated, for Whatman No. 1 paper, with (I) M/50-KH_2PO_4; (II) M/50-Na_2HPO_4; both at 10 v/cm. for 2 hr. Results (cm.) were as shown.

	I	II
Adenosine-2′(3′) phosphate	5·6	8·9
Adenosine-2′ : 3′ cyclic phosphate	5·2	5·9
5′-Methanesulphonyladenosine-2′ : 3′ cyclic phosphate	4·9	5·9
*cyclo*Adenosine-2′ : 3′ cyclic phosphate	2·6	3·1
Uridine-3′ phosphate	7·2	10·5
Uridine-2′ : 3′ cyclic phosphate	6·8	7·8
5′-Methanesulphonyluridine-2′(3′) phosphate	7·2	9·8

Movement of the polymer dialysis residues in solvent (I) at 25 v/cm. for 75 min. and solvent (III), 0·05M-ammonium formate, at 13 v/cm. for 2 hr., is tabulated, for Whatman No. 1 paper:

	I	III
Adenosine-2′(3′) phosphate	9·2	6·3
Polyadenylic acid	11·3	7·1
Polyadenylic-uridylic acid (4·5 : 1)	11·4	7·1
Polyadenylic-uridylic acid (1·4 : 1)	11·7	—
Polyadenylic-uridylic acid (1 : 1·25)	12·1	—
Polyuridylic acid	12·5	10·1
Uridine-2′(3′) phosphate	10·0	8·4
Synthetic " ribonucleic acid "	—	6·8 streak
Yeast ribonucleic acid	—	6·8 streak

Electrophoretic separation in solvent (III) at pH 3·5 at 17 v/cm. for 2 hr. showed no apparent combination between polyadenylic (8·2 cm.) and polyuridylic acid (10·1 cm.) [cf. mixture of polymers (8·1 and 10·1 cm.); copolymer of adenylic and uridylic acids (9·4 cm.)].

Analyses (Mr. W. Byrne).—In view of the nature of the compounds, no general attempt was made to obtain completely anhydrous materials.

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Compound	Average chain length	After drying at 60°/10^{-3} mm. 12 hr. Found N (%)	Found P (%)	Reqd. in anhyd. material N (%)	P (%)	Molar ratios N : P Found	Reqd.
Poly A	9·1	19·4	8·6	21·3	9·4	5·0	5·0
Poly A	7·7	19·3	8·4	21·3	9·4	5·1	5·0
Poly A	3·3	19·5	8·3	21·3	9·4	5·2	5·0
Poly A (dried at 100°)	—	20·0	9·1	21·3	9·4	4·9	5·0
Poly G	5·4	18·1	8·2	20·3	9·0	4·9	5·0
Poly G	3·2	17·4	8·1	20·3	9·0	4·8	5·0
Poly U Ca	8·2	8·6	9·1	8·6	9·5	2·1	2·0
Poly U Ca	6·6	7·7	8·4	8·6	9·5	2·0	2·0
Poly U Ca	3·5	7·6	8·2	8·6	9·5	2·05	2·0
Poly U Ca (dried at 100°)	—	8·4	9·3	8·6	9·5	2·0	2·0
Poly ACGU	5·2	15·7	8·7	—	—	4·0	—
Poly ACGU	3·2	16·9	9·1	—	—	4·1	—
Yeast RNA	5·1	15·5	9·1	—	—	3·8	—
RNAase resistant cores	6·2	17·1	8·5	—	—	4·5	—

Analyses are tabulated but results for other polymers prepared were as follows. Poly AU (4·5 : 1): N, 17·6; P, 8·9. Poly AU (4·5 : 1); N, 18·5; P, 9·5. Poly AU (1·4 : 1): N, 16·6; P, 9·2; Poly AU (0·8 : 1): N, 14·8; P, 9·5. Poly AU (0·8 : 1): N, 14·6; P, 9·3. Poly AU (3·1 : 1): N, 16·5; P, 8·7. Poly AU (0·12 : 1)Ca: N, 8·5; P, 8·3. P5′U Poly A (13·5 : 1): N, 18·8; P, 9·2. P5′U Poly A (10·4 : 1): N, 18·6; P, 9·0. P5′U Poly U Ca (16 : 1): N, 7·6; P, 9·1. P5′U Poly U Ca (12·5 : 1): N, 7·4; P, 9·1%.

Action of Polynucleotides on the Absorption Spectra of Rosaniline, Toluidine Blue, and Acridine Orange.—Stock solutions of the dyes (10^{-4}M), polynucleotides (10^{-4}M with respect to phosphorus), and ammonium acetate (0·1M; pH 6·8) were mixed and diluted to give solutions for spectroscopic examination which were 2×10^{-5}M with respect to Rosaniline and polynucleotide and 3×10^{-5}M in the case of Toluidine Blue and Acridine Orange. All solutions were 0·01M with respect to ammonium acetate. No metachromasy was observed with adenosine-2′(3′) phosphate, adenosine-2′ uridine-5′ phosphate, adenylic-cytidylic dinucleotide (A3′P5′C3′P), or polyglycerophosphoric acid (average chain length ~12). The effects of the other polymers (average chain length ~6) are shown in Figs. 8—10. Spectra were measured on a Perkin-Elmer recording spectrophotometer (Spectracord model 4000).

Quenching of the Fluorescence of Acridine Orange.—The fluorescence of Acridine Orange (3×10^{-5}M) in 0·01M-ammonium acetate at pH 6·8 in the presence of 3×10^{-5}M(P)-polynucleotide was measured in a Beckman fluorimeter. Average chain length of the polymers both natural and synthetic was ~6 in all cases except for polyglycerophosphate (12·2). The results are expressed as a percentage of the fluorescence of Acridine Orange in the absence of polymer.

Substance	Fluorescence
Acridine orange alone	100
Polyglycerophosphate	99·5
Adenosine-2′(3′) phosphate	99
A2′P5′U	99
A3′P5′C3′P	98
Poly U	86
Poly ACGU	75
Poly A	62
Poly G	52
Poly AG	46
RNAase resistant core	37
Yeast RNA	30

Spectrophotometric Titrations.—Determinations of pH were made on an E.E.L. direct reading pH meter and of ultraviolet absorption density on a Beckman DU spectrophotometer. Apparent pK's were calculated by using the expression $pK_a = pH - \log (\varepsilon_{HA} - \varepsilon)/(\varepsilon - \varepsilon_A)$, with the following results. Guanosine-2(3′) phosphate, 2·32 and 9·33; polyguanylic acid (average chain length 5·4), 2·63 and 10·76; polyguanylic acid (average chain length 12·5), 11·20. Acid titrations were made at 290 mμ and alkaline ones at 270 mμ to utilise maximum optical changes. With polyadenylic-guanylic acid (2·0 : 1) over the range pH 8—13 at 290 mμ

a shift to pK 10·5 was noted (owing, however, to the ill-defined slope of the curve, possibly due to the various combinations in the mixed polymer, this is not necessarily accurate). The polyuridylic acids gave only slight changes in the apparent pK's associated with the 6-position of the pyrimidine ring, measurements being made between pH 7 and 13 at 260 mμ. Similar measurements on adenosine-2′ uridine-5′ phosphate at 270 mμ (near the isosbestic point of adenosine) indicated no significant change in pK_a (9·65).

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Arthur Guinness Son & Co. (Dublin) Ltd.,
Dublin, Ireland.

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271. *The Structure of the α-Modification of* 1 : 4-*Dithian* 1 : 4-*Dioxide.*

By H. M. M. Shearer.

The crystal structure of this dioxide has been determined by X-ray methods. The monoclinic unit cell, $a = 6{\cdot}34 \pm 0{\cdot}01$, $b = 6{\cdot}46 \pm 0{\cdot}01$, $c = 8{\cdot}22 \pm 0{\cdot}01$ Å, $\beta = 103° 57' \pm 15'$, space-group $P2_1/n$, contains two centrosymmetrical molecules. Analysis of the three principal zones leads to a model in which the dithian ring has the chair form with the oxygen atoms in the *trans*-diaxial positions. No unusual bond distances or intermolecular contacts are found.

Bell and Bennett [1] reported that oxidation of 1 : 4-dithian gave two dioxides or disulphoxides. That produced in greater yield, designated α, was described as being more soluble in water and less soluble in ethanol than the other (β). The authors suggested that it was the *trans*-compound. The present work confirms this and shows that the molecules, in crystals of the α-form, have the *trans*-diaxial configuration with the ring in the chair conformation, as in the parent compound 1 : 4-dithian [2,3] itself.

Crystal Data.—Monoclinic; $a = 6{\cdot}34 \pm 0{\cdot}01$, $b = 6{\cdot}46 \pm 0{\cdot}01$, $c = 8{\cdot}22 \pm 0{\cdot}01$ Å, $\beta = 103° 57' \pm 15'$. $U = 326{\cdot}7$ Å^3, $D_m = 1{\cdot}535$ g. cm.$^{-3}$, $Z = 2$, $D_c = 1{\cdot}547$ g. cm.$^{-3}$, μ ($\lambda = 0{\cdot}7107$ Å) $= 7{\cdot}37$ cm.$^{-1}$. Space-group $C_{2h}{}^5$–$P2_1/n$ from systematic absences. Molecular symmetry, centre.

Experimental

Crystals were obtained as thin plates, with the {10$\bar{1}$} and {101} faces well developed, by evaporation from a solution in ethanol. The unit-cell dimensions were measured from precession photographs and the axial ratios (0·981 : 1 : 1·272) were found to be in good agreement with those given by Bell and Bennett [1] (0·979 : 1 : 1·267; $\beta = 104° 3'$).

For intensity measurements a crystal of cross-section 0·20 × 0·23 mm. and length 0·80 mm. was used, mounted about the b axis. The ($h0l$) reflections were recorded on an integrating Weissenberg apparatus, and the ($hk0$) and ($0kl$) reflections on the precession camera; Zr-filtered Mo radiation was used throughout. The intensities were estimated visually, an exposure scale being used, and corrected for the usual angle factors. No corrections were applied for absorption.

Structure Determination.—The space-group is $P2_1/n$ with two molecules in the unit cell, so that the molecule possesses a centre of symmetry. It must therefore have the chair configuration with the oxygen atoms in diaxial or diequatorial positions.

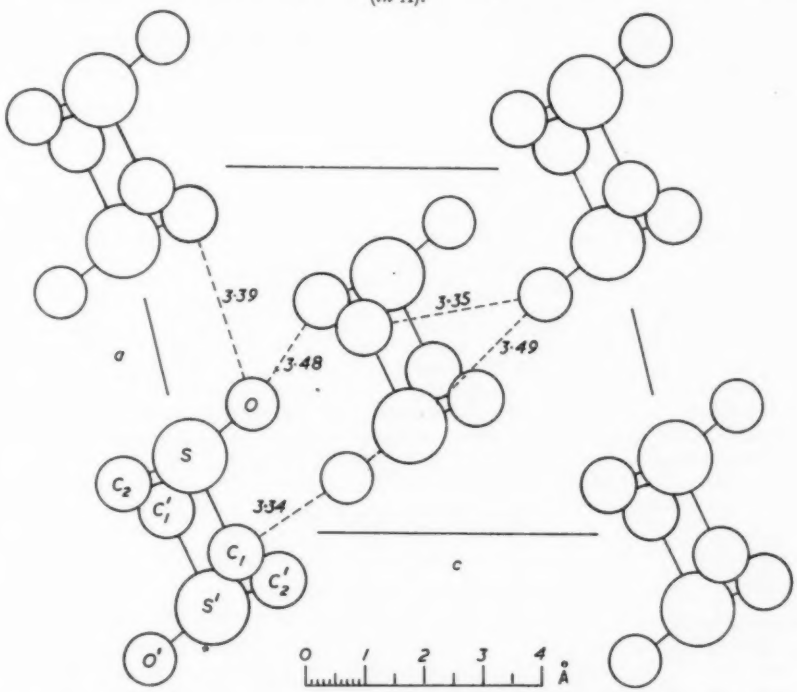
The (010) projection was examined first since this was the simplest. The sharpened Patterson function was evaluated, by using as coefficients $F^2/\sum f^2$. The Patterson map showed two large peaks of almost equal height. One was sharper and rounder than the other with an

[1] Bell and Bennett, *J.*, 1927, 1798.
[2] Duthie, *Acta Cryst.*, 1953, **6**, 804.
[3] Marsh, *ibid.*, 1955, **8**, 91.

environment similar to that at the origin and so was taken as the S–S vector across the centre of symmetry. A single superposition, with the origin of the Patterson function transferred to this point, gave approximate positions for the carbon and oxygen atoms in this projection and showed the oxygen atoms to be diaxial.

Refinement was carried out by means of one F_o and two F_o–F_c syntheses, and the contributions of the hydrogen atoms (the positions of which were estimated approximately from a model) were included in the final stage. The arrangement of the atoms in this projection is shown in Fig. 1.

FIG. 1. *Arrangement of the molecules in the* (010) *projection with the shortest intermolecular distances* (*in* Å).



For the (001) projection, the determination of the approximate structure and its refinement were carried out in a similar manner. In the (100) projection, considerable overlapping of the atoms occurs and only a final structure factor calculation was made as a check of the correctness of the structure.

The structure factors were calculated by using the form factor due to Viervoll and Ogrim [4] for the sulphur atoms, those of Hoerni and Ibers [5] for the carbon and oxygen atoms, and that of McWeeny [6] for hydrogen. On the basis of the difference maps, individual temperature factors were assigned to the different atomic species and the final values of the exponent B (in Å^2) in the expression exp $(-B \sin^2\theta/\lambda^2)$ are shown below.

	S	O	C		S	O	C		S	O	C
(*h*0*l*) ...	3·1	3·4	3·3	(*hk*0) ...	3·1	4·0	3·7	(0*kl*) ...	3·1	3·8	3·5

The value of $B = 3{\cdot}5$ Å^2 for the hydrogen atoms was adopted, somewhat arbitrarily, for all the structure factors. The reliability indices were 9·8% for the (*h*0*l*) reflections, 9·0% for the (*hk*0), and 9·1% for the (0*kl*). The structure factors are listed in Table 3.

[4] Viervoll and Ogrim, *Acta Cryst.*, 1949, **2**, 277.
[5] Hoerni and Ibers, *ibid.*, 1954, **7**, 744.
[6] McWeeny, *ibid.*, 1951, **4**, 513.

XUM

The final atomic co-ordinates are given in Table 1 and the bond lengths and angles in Table 2 with their averaged values in Fig. 2. Estimates of the standard deviations in bond lengths and angles were calculated [7] and are included in Table 3.

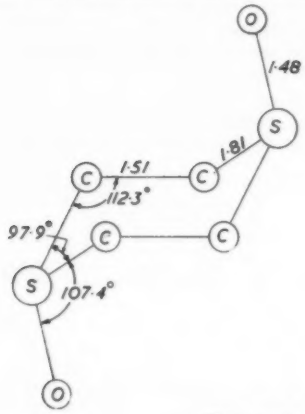


FIG. 2. *Averaged molecular dimensions (in* Å).

TABLE 1. *Atomic co-ordinates.*

	x/a	*y/b*	*z/c*		*x/a*	*y/b*	*z/c*
S	0·207	0·181	0·016	H_1	−0·141	0·224	−0·050
O	0·350	0·095	0·170	H_2	−0·070	0·340	0·163
C_1	−0·058	0·219	0·061	H_3	0·281	−0·065	−0·190
C_2	0·133	−0·025	−0·134	H_4	0·027	0·031	−0·237

TABLE 2. *Bond lengths* (Å) *and angles.*

S–O	1·48 ± 0·014	S–C_2	1·80 ± 0·018	C_1–S–O	106·4° ± 0·8°	C_2'–C_1–S	111·2° ± 1·25°
S–C_1	1·82 ± 0·018	C_1–C_2'	1·51 ± 0·025	C_2–S–O	108·3° ± 0·8°	C_1'–C_2–S	113·3° ± 1·25°
				C_1–S–C_2	97·9° ± 0·8°		

TABLE 3. *Structure factors.*

hkl	F_o	F_c	*hkl*	F_o	F_c	*hkl*	F_o	F_c	*hkl*	F_o	F_c	*hkl*	F_o	F_c	*hkl*	F_o	F_c
200	36·0	−32·3	307	14·0	−17·3	606	<2·7	+0·8	320	13·2	+13·6	012	34·4	−33·7	047	4·9	+6·1
400	1·8	−2·2	205	17·9	−18·8	608	3·6	−2·3	330	10·2	+9·6	013	13·0	−10·8	048	<2·1	+0·1
600	4·0	+3·1	303	38·8	−42·6				340	15·8	−15·9	014	9·1	−9·6	049	2·9	+4·1
800	3·3	−3·2	301	23·3	−23·3	705	9·9	−10·4	350	15·5	−14·4	015	9·4	+11·1	0,4,10	1·4	−1·2
			301	12·9	−11·0	703	8·9	−8·7	360	7·4	+7·6	016	10·0	−13·3			
020	20·2	−18·6	303	11·4	−8·5	701	10·0	−10·0				017	8·0	+9·1	051	20·3	+18·8
040	1·9	−1·4	305	2·3	+1·8	701	11·5	−10·4	410	19·7	+22·0	018	8·0	−10·1	052	4·4	−3·4
060	9·7	+9·4	307	3·9	−3·4	703	5·3	−5·8	420	12·0	−13·3				053	16·9	+18·2
080	7·1	−6·3				705	4·3	−3·8	430	11·6	−12·2				054	3·0	+2·7
			408	3·1	−3·0				440	2·1	−1·2	021	26·0	−25·9	055	5·7	+5·5
002	42·1	+38·8	406	9·9	−12·2	808	2·8	−3·4	450	4·7	−5·4	022	43·7	−40·5	056	2·9	+3·9
004	13·7	+13·7	404	<1·7	+1·3	806	2·6	−3·3	460	4·4	+4·4	023	13·0	−11·3	057	4·3	+4·4
006	21·4	+23·0	402	13·3	+12·9	804	7·5	−6·1	470	6·7	+6·2	024	26·1	−24·5	058	<2·0	+2·0
008	5·4	+5·8	402	18·3	+16·8	802	9·7	−9·1	480	1·7	−2·3	025	2·1	−2·0	059	3·3	+3·2
			404	26·9	+23·3	802	<2·7	−1·2				026	2·7	−3·6			
10$\bar{5}$	5·1	+7·3	406	7·3	+7·6	804	2·9	−2·2				027	9·7	−11·3			
107	14·9	+16·9	408	4·1	+4·4				510	4·6	+5·1	028	<2·2	−1·3	061	3·2	−2·1
105	5·6	+5·6	4,0,10	3·6	+3·3	10,0,$\bar{4}$	4·6	+4·0	520	2·1	+2·3	029	4·0	−5·1	062	12·3	+12·4
10$\bar{3}$	18·2	+20·9							530	13·5	−15·2	0,2,10	2·0	−2·1	063	6·4	−5·8
101	42·3	+45·2	5,0,$\bar{11}$	4·3	+5·3	110	8·4	+9·5	540	<1·8	+2·0				064	7·9	+8·6
101	27·0	+25·4	509	7·4	+8·2	120	40·6	−39·5	550	7·3	+6·9				065	4·3	−3·4
103	16·5	+19·2	507	3·1	+4·0	130	3·4	−3·8				031	30·7	−29·5	066	4·4	+4·7
105	8·0	−8·4	505	13·1	+14·3	140	20·0	+19·3	610	11·6	−11·4	032	9·7	−10·2	067	2·3	−1·7
107	10·8	−12·1	503	18·0	+18·6	150	14·0	+13·8	620	1·8	+2·9	033	30·9	−29·8	068	3·9	+5·0
109	2·9	−3·4	501	11·7	+11·0	160	3·1	−2·6	630	1·8	−1·2	034	15·4	+16·2			
1,0,11	3·9	−4·4	501	21·6	+18·8	170	1·7	−0·9	640	<1·8	−1·7	035	15·9	−18·1			
			503	14·8	+13·6				650	3·1	+3·5	036	6·1	+5·3	071	5·0	−3·4
20$\bar{5}$	8·5	−9·4	505	9·7	+9·3	210	4·5	+6·8				037	4·6	−6·0	072	2·3	−1·8
20$\bar{6}$	10·2	−12·4	507	6·6	+5·5	220	8·5	+9·0	710	4·1	−3·7	038	<2·2	−0·5	073	2·3	−1·3
20$\bar{4}$	5·2	−3·9				230	14·5	+15·7	720	1·8	−2·5	039	2·8	−2·9	074	2·9	−4·1
20$\bar{2}$	58·4	−56·8				240	7·8	+7·7	730	10·2	+8·9	0,3,10	1·7	+1·5	075	<2·0	−1·0
202	4·9	+6·0	6,0,$\bar{10}$	4·3	+4·9	250	9·4	+10·2	740	<1·7	+1·1				076	1·7	−1·7
204	30·4	−28·2	606	7·8	+7·7	260	10·7	−10·0	750	3·2	−3·4	041	5·9	−5·8	077	1·2	+0·8
206	21·4	−21·2	606	4·7	+6·1	270	4·7	−5·2	810	6·6	+5·4	042	2·6	+2·6			
208	6·2	−7·4	604	2·6	−2·3	280	5·1	+5·4	820	5·8	+3·7	043	9·1	+8·1	081	<1·9	+0·9
2,0,10	4·9	−5·8	602	4·8	+4·1							044	3·6	−2·7	082	6·7	−6·4
			602	7·1	−6·8							045	15·7	+15·4	083	<1·8	−0·2
30$\bar{5}$	12·8	−14·8	604	<2·3	−0·6	310	2·9	−3·3	011	49·3	+50·4	046	4·6	−5·4	084	4·6	−5·3

[7] Cruickshank and Robertson, *Acta Cryst.*, 1953, **6**, 698.

Application of statistical tests shows that the differences between the chemically equivalent bonds S–C_1, S–C_2 and the equivalent angles C_1–S–O, C_2–S–O and C_1'–C_2–S, C_2'–C_1–S are not significant; nor do the dimensions of the dithian ring differ significantly from these obtained for dithian itself.[3] The dimensions of the sulphoxide group are similar to those found in other compounds.[3]

The shortest van der Waals contacts are of 3·34, 3·35, and 3·39 Å between the oxygen atom of one molecule and carbon atoms of adjacent molecules. All the intermolecular distances of less than 3·75 Å are shown in Fig. 1.

The author thanks Dr. G. M. Bennett for a sample of the pure compound, and Dr. J. D. Dunitz for his interest and suggestions throughout the work.

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[*Received, October 28th*, 1958.]

[3] Abrahams, *Quart. Rev.*, 1956, **10**, 407.

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272. *Di(tertiary Arsine) Iron Carbonyls and Oxidation Products.*

By H. NIGAM, R. S. NYHOLM, and D. V. RAMANA RAO.

When treated with the di(tertiary arsine), *o*-phenylenebisdimethylarsine, iron pentacarbonyl gives two new compounds, $Fe(CO)_3$Diarsine and $FeCO(Diarsine)_2$. These are both monomeric and are virtually non-electrolytes in nitrobenzene solution. On treatment with iodine, under carefully controlled conditions, the paramagnetic univalent iron complex $[Fe(CO)_2$DiarsineI$]^0$ is formed; this is monomeric in nitrobenzene and a non-electrolyte, showing that the iron atom is quinquecovalent. Further addition of iodine, or the use of bromine, yields $[Fe(CO)_2$Diarsine $X_2]^0$ (X = Br,I). The compound $[Fe(CO)(Diarsine)_3]^0$ yields only the known complex $[Fe(Diarsine)_3I_2]^0(Br_2)$ on treatment with iodine or bromine. The reaction of the zerovalent iron compounds with nitric oxide has been investigated.

THE replacement of one or more CO groups from iron pentacarbonyl has been effected previously with a variety of ligands forming compounds of the type $[Fe(CO)_n(Ligand)_{5-n}]^0$. These include tertiary phosphines, arsines, and stibines, the *iso*nitriles and certain amines like dipyridyl and *o*-phenanthroline.[1] Practically all of the ligands which can replace the CO group to give mixed carbonyls are at least theoretically capable of forming, in addition to the usual σ bonds, dative π bonds using *d*-electron pairs of the metal fed into a vacant *d* (or *p* orbital made available) on the ligand atom. Exceptions include ammonia, ethylenediamine, and certain tertiary amines. However, there is now considerable doubt as to whether certain compounds formed by these ligands really are mixed iron amine carbonyls. Thus, recent work has shown that $Fe_3(CO)_8(NH_3)_6$,[2] formerly believed to have the composition $Fe(CO)_3(NH_3)_2$, is actually a salt of the type $[Fe(NH_3)_6][Fe_2(CO)_8]$. Even certain *o*-phenanthroline compounds [3] appear not to be direct substitution products; conductivity measurements and other studies show that the salt $[Fe(o\text{-phen})_3][Fe_2(CO)_8]$ is formed. Similarly the ethylenediamine compounds are apparently salts also.[4]

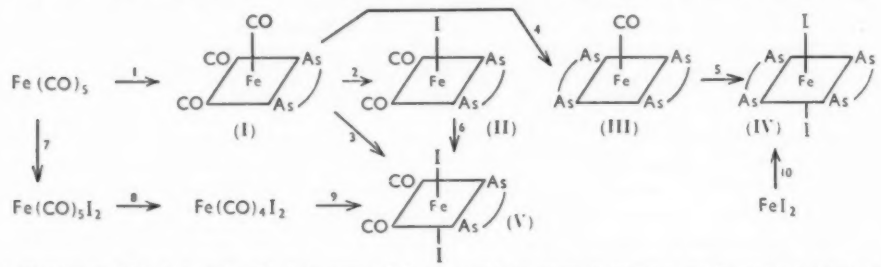
The use of chelate groups for the direct replacement of CO is of special interest because of the expected stability of the products owing to the entropy effect and also because they necessarily replace CO groups in *cis*-positions. In view of the powerful co-ordinating

[1] See Review by Hieber, *Angew. Chem.*, 1952, **64**, 465.
[2] Hieber and Werner, *Chem. Ber.*, 1957, **90**, 1116.
[3] Hieber and Floss, *Chem. Ber.*, 1957, **90**, 1617.
Hieber, Sedlmeier, and Werner, *Chem. Ber.*, 1957, **90**, 278.

ability of the chelating di(tertiary arsine), *o*-phenylenebisdimethylarsine [5,6], its behaviour with iron pentacarbonyl has been investigated.

With nickel carbonyl, the compound $Ni(CO)_2$Diarsine is formed readily [7] by displacing two CO groups. Recently [8] we have found that the remaining CO groups can be displaced by heating this compound with diarsine *in vacuo* to yield $[Ni(Diarsine)_2]^0$ as a white crystalline compound similar to the corresponding bisdiphosphine compound prepared by Chatt and Hart.[9] Considerable interest attaches to the use of a diarsine chelate group in substitution reactions with $Fe(CO)_5$ as it was hoped that four CO groups might be replaced; previously a maximum of three only appears to have been substituted.

When iron pentacarbonyl and the diarsine are heated *in vacuo* at about 140° for about 4 hr., two CO groups are replaced readily to yield a golden-yellow crystalline compound having the formula $Fe(CO)_3$Diarsine. This is monomeric in organic solvents and is a non-electrolyte in nitrobenzene. Further heating of this compound with diarsine causes further substitution yielding $Fe(Diarsine)_2CO$. This is also monomeric and a non-electrolyte in nitrobenzene. Both compounds are more stable to light than is $Fe(CO)_5$; even so they gradually darken on standing. The bisdiarsine monocarbonyl is the less stable of the two as is reflected in the analysis and the conductivity. The properties of these compounds are shown in the diagram; for convenience, both substitution products are shown as square pyramidal; there is no experimental evidence for favouring this shape over trigonal bipyramidal which is generally accepted for $Fe(CO)_5$, although some doubt remains as to whether this is correct. Electron-diffraction work first led to the adoption of this structure; the small electric dipole moment 0·6—0·8D can scarcely be used with any confidence to differentiate between the two shapes in view of the uncertainty as to atom polarisation. To obtain best results from spectroscopy both infrared and Raman data are desirable. The infrared spectrum is well known but the determination of the Raman spectrum is difficult owing to the ease with which $Fe(CO)_5$ polymerises in ultraviolet light; there have recently been conflicting conclusions based on these data. Thus, Sheline and



1, Diarsine at 130°; 2, 1 equiv. of I_2 in benzene; 3, 2 equiv. of I_2 in ether; 4, Diarsine at 140—150°; 5, 2 equiv. of I_2 in ether; 6, I_2 in benzene; 7, I_2 below 0°; 8, above 0°; 9, Diarsine; 10, Diarsine in alcohol.
(I) Yellow, m. p. 131°; (II) brown-yellow, decomp. 195°; (III) brown-yellow, m. p. 150°; (IV) orange-yellow; (V) brown, m. p. 186°.

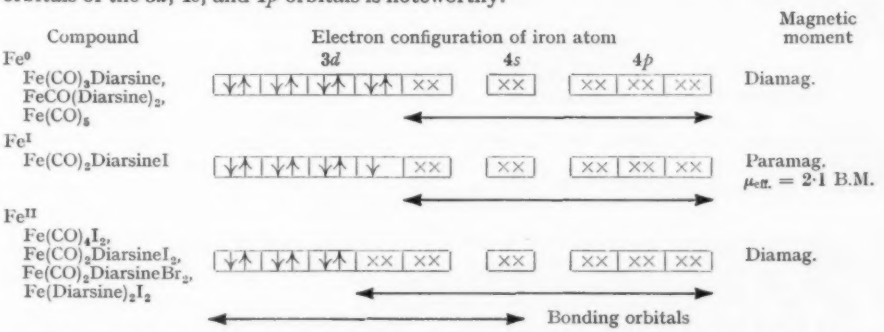
Pitzer [10] satisfactorily assigned all the infrared frequencies of gaseous $Fe(CO)_5$ on the basis of a trigonal bipyramid. In addition to the infrared, King and Lippincourt [11] also measured the Raman spectrum of a dilute solution in *n*-hexane using sodium light and agreed with Sheline and Pitzer's conclusions. Recently, however, O'Dwyer [12] re-assigned the infrared frequencies and concluded that the molecule is a square pyramid. Even if

[5] Chatt and Mann, *J.*, 1939, 610.
[6] See Nyholm and Sutton, *J.*, 1958, 560 for references.
[7] Nyholm, *J.*, 1951, 2906.
[8] Nyholm and Rao, unpublished work.
[9] Chatt and Hart, *Chem. and Ind.*, 1958, 1474.
[10] Sheline and Pitzer, *J. Amer. Chem. Soc.*, 1950, **72**, 1107.
[11] King and Lippincourt, *J. Amer. Chem. Soc.*, 1956, **78**, 4192.
[12] O'Dwyer, *J. Mol. Spectroscopy*, 1958, **2**, 144.

$Fe(CO)_5$ is unambiguously shown to be a trigonal bipyramid, this will not necessarily mean that substituted iron carbonyls will have this shape. It may well be that the presence of different degrees of d_π–d_π bonding and steric effects generally could change the preferred stereochemistry. The crystal structures of $Fe(CO)_3$Diarsine and $FeCO(Diarsine)_2$ are being studied by *X*-rays by Mr. H. M. Powell, F.R.S., and his collaborators in the Inorganic Chemistry Laboratory at Oxford.

The behaviour of these substituted carbonyls with halogens leads to a series of very interesting new compounds. Treatment of $Fe(CO)_3$Diarsine with excess of iodine in absolute ether gives rise to a diamagnetic compound having the empirical formula $[Fe(CO)_2DiarsineI_2]$, monomeric in organic solvents and a non-electrolyte in nitrobenzene. It is clearly an octahedral spin-paired complex as shown in the diagram; we show the two CO groups as *cis* for convenience only since no experimental evidence for these assignments is available. The corresponding dibromide $[Fe(CO)_2DiarsineBr_2]$[0] can be prepared by use of bromine as the oxidising agent. Unfortunately the corresponding chloro-complexes could not be isolated, presumably owing to high reactivity of the chloro-derivatives (cf. attempts[7] to prepare $NiDiarsineCl_2$). These complexes are clearly analogous with the iron compound $Fe(CO)_2(Pyridine)_2I_2$ described by Hieber and Bader[13] and the ruthenium compounds $Ru(CO)_2L_2I_2$ (L = CH_3AsPh_2, aniline, etc.) prepared by Irving.[14] These can be formed by treating $Ru(CO)_2I_2$, which is a red insoluble material, with a large excess of the ligand. The resulting compounds are monomeric and diamagnetic. The compound $Fe(CO)_2DiarsineI_2$ can be prepared also by treating $Fe(CO)_4I_2$ with diarsine. The product is identical with that obtained from the action of iodine on $Fe(CO)_3$Diarsine.

If $Fe(CO)_3$Diarsine is treated with only one equivalent of iodine under carefully controlled conditions it is possible to isolate a product having the empirical formula $Fe(CO)_2DiarsineI$. This is obtained by carefully avoiding local concentrations of iodine and by carrying out the reaction in the cold. The monoiodide is virtually a non-electrolyte in nitrobenzene and is monomeric in such solvents, suggesting that the iron atom is quinquecovalent, having an oxidation state of +1. This is confirmed by the magnetic moment (2·1 B.M.), indicating one unpaired electron. The relationship between the electronic configuration of this compound, the zerovalent iron compounds, and the bivalent derivatives is shown in the annexed scheme; the desire of the iron atom to use all nine orbitals of the 3*d*, 4*s*, and 4*p* orbitals is noteworthy.



The oxidation state of +1 for iron is very unusual; it has been reported previously in $Fe(CO)_2I$ and in some nitric oxide complexes of iron.[14a] According to Hieber and Lagally[15] the former is obtained by heating $Fe(CO)_4I_2$ in carbon dioxide. However, $Fe(CO)_2I$ was not obtained pure owing to its instability. It was reported that on further

[13] Hieber and Bader, *Ber.*, 1930, **63**, 1405.
[14] Irving, *J.*, 1956, 2879.
[14a] Griffith, Lewis, and Wilkinson, *J.*, 1958, 3993.
[15] Hieber and Lagally, *Z. anorg. Chem.*, 1940, **245**, 295; 1943, **251**, 96.

heating it yielded FeI as a very reactive red powder. Magnetic data are not available for these compounds. A second feature of interest is the fact that the compound contains quinquecovalent iron. This co-ordination number is relatively uncommon with the transition metals but it is relevant that an isoelectronic series of paramagnetic, quinquecovalent complexes exist having a d^7 non-bonding shell (*i.e.*, for Mn^0, Fe^I, Co^{II}, and Ni^{III}). Thus Mn^0 forms $Mn(CO)_4PPh_3$ which has one unpaired electron and is monomeric;[16] Co^{II} forms several paramagnetic, presumably quinquecovalent complexes, *e.g.*, $K_3Co(CN)_5$[17] and $[CoBr_2,Triarsine]^0$;[18] also, Ni^{III} gives derivatives such as $[NiBr_3,2Et_3P]^0$[19,20] which is monomeric in benzene and also contains one unpaired electron. $NiBr_3$,Diarsine[7] is undoubtedly similar. Since Jensen's studies on $NiBr_3,2Et_3P$ there has been much speculation as to the stereochemistry of this quinquecovalent compound. If the $d_{x^2-y^2}$ orbital hybridises with the *s* and *p*, then a square pyramid will result. However, use of the d_{z^2} orbital should give a trigonal bipyramid. Generally speaking the former seems the more likely. By adding one electron one gets another isoelectronic sequence of quinquecovalent compounds: Fe(O), *e.g.*, $Fe(CO)_5$; Co^I, *e.g.*, $[Co(RNC)_5]^+X^-$,[21] and Ni^{II}, *e.g.*, $NiBr_2$,Triarsine.[18] The earlier discussion on whether these are square pyramidal or trigonal bipyramidal resolves itself into the question of whether the lone pair is in the $d_{x^2-y^2}$ or d_{z^2} orbital and although the latter seems definite for the Ni^{II} compounds at least, conclusions based upon this compound will not necessarily have any relevance for $Fe(CO)_5$. Another interesting point about $Fe(CO)_2$DiarsineI is that it is one of the very few known paramagnetic substituted metal carbonyls. All non-substituted carbonyls are diamagnetic; apparently the strong tendency of CO to cause the metal to reach the inert gas configuration is outweighed if the number of remaining CO groups is sufficiently small (in this compound 2) and other influences become more important.

When $FeCO(Diarsine)_2$ is treated with two equivalents of iodine, the CO group is lost to yield the bivalent iron compound $[Fe(Diarsine)_2I_2]^0$ previously obtained[22] by treating ferrous iodide with the diarsine in alcohol. It is a typical diamagnetic octahedral Fe^{II} complex. Treatment with bromine gives the corresponding diamagnetic dibromide. In no case were we able to obtain any carbonyl diarsine complexes of tervalent iron. Ferric salts could be obtained by treating the zerovalent carbonyl diarsine compounds with chlorine but in these all carbon monoxide had been displaced.

The infrared frequencies of the various compounds which can be confidently assigned to CO stretching are given in the Table. $FeCo(Diarsine)_2$ gives only one CO stretching

Compound	Infrared frequencies attributed to C–O stretching (In Nujol mull)	Compound	Infrared frequencies attributed to C–O stretching. (In Nujol mull)
$Fe^0(CO)_5$ *	2028, 1994	$Fe^{II}(CO)_2DiarsineI_2$	2062vs, 2008vs
$Fe^0(CO)_3$Diarsine	2009vs, 1916vs, 1880sh	$Fe^{II}(CO)_2DiarsineBr_2$	2083vs, 2008s
$Fe^0(CO)(Diarsine)_2$	1953s	$Fe^{II}(Diarsine)_2I_2$	Nil
$Fe^I(CO)_2$DiarsineI	2083s 2024s, 1976w		

* Sheline and Pitzer (ref. 10).

frequency, as expected if only one CO is present. The similarity of the $Fe(CO)_2DiarsineBr_2$ and $Fe(CO)_2DiarsineI_2$ spectra is apparent as is also the difference between these and that of $Fe(CO)_2$DiarsineI.

The behaviour of the monodiarsine complex with nitric oxide has also been investigated. Malatesta and Araneo[23] showed that complexes of the type $Fe(Ph_3P)_2(NO)_2$ can be obtained

[16] Hieber and Wagner, *Z. Naturforsch.*, 1957, **12**b, 478.
[17] Adamson, *J. Amer. Chem. Soc.*, 1951, **73**, 5710.
[18] Barclay and Nyholm, *Chem. and Ind.*, 1953, 378.
[19] Jensen, *Z. anorg. Chem.*, 1936, **229**, 265.
[20] Jensen and Nygaard, *Acta Chem. Scand.*, 1949, **3**, 474.
[21] Malatesta and Sacco, *Z. anorg. Chem.*, 1953, **273**, 247.
[22] Nyholm, *J.*, 1950, 851.
[23] Malatesta and Araneo, *J.*, 1957, 3803.

by treating $Fe(CO)_3(Ph_3P)_2$, which is equivalent to $Fe(CO)_3$Diarsine, with nitric oxide. This involves the usual behaviour in which the two NO groups replace three CO or one CO and the metal–metal link. When $Fe(CO)_3$Diarsine in benzene was treated with a stream of dry nitric oxide for some hours a clear solution was obtained from which an off-white material was precipitated on the addition of light petroleum. Unfortunately, since some decomposition products are formed in addition to what is probably $Fe(NO)_2$Diarsine, this could not be obtained pure.

The compounds prepared are shown in the diagram together with their interconversions. It is noteworthy that iron has now been stabilised with the di(tertiary arsine) in all the oxidation states from 0 to IV, the tervalent [24] complexes being of the general type $[Fe^{III}Cl_2(Diarsine)_2]ClO_4$ and the quadrivalent $[Fe^{IV}Cl_2(Diarsine)_2][ClO_4]_2$.

Experimental

Mono-o-phenylenebisdimethylarsinetricarbonyliron(0).—Iron pentacarbonyl (1·5 g.) and diarsine (2·5 g.) were mixed in a hard-glass tube (length 12 in., diam. 1 in.), the tube and the contents were cooled in liquid nitrogen, and the tube was evacuated and sealed, then heated at 130—140° for 3—4 hr. On cooling the tube was opened carefully owing to the CO pressure and the golden-yellow crystalline *product* was washed with dry light petroleum and recrystallised (ether). Dried *in vacuo* (3·5 g.), the compound melted at 131° (Found: C, 36·5; H, 3·9; As, 35·1; Fe, 13·4%; *M*, cryoscopic in 0·51% solution in benzene, 401. $C_{13}H_{16}O_3As_2Fe$ requires C, 36·64; H, 3·76; As, 35·2; Fe, 13·2%; *M*, 426). The compound is readily soluble in all common organic solvents and sparingly soluble in light petroleum. It is fairly stable in a dry, dark and inert atmosphere. In solution it is unstable in presence of air, a brown precipitate being formed gradually. It is a poor conductor in nitrobenzene ($\Lambda_m = 3$ mho in $1{\cdot}01 \times 10^{-3}$M-solution at 25°. This figure increases with time, indicating decomposition). The compound is diamagnetic ($\chi_g = -0{\cdot}15 \times 10^{-6}$ at 21°).

Bis-o-phenylenebisdimethylarsinemonocarbonyliron(0).—The monosubstituted diarsine complex FeDiarsine$(CO)_3$ (1·59 g.) and diarsine (1·0 g.) were mixed as before in a hard-glass tube and evacuated and sealed. The tube was then heated at 140—150° for 3—4 hr. The CO liberated was then pumped off and the process of heating repeated four times. The *compound* was recrystallised from the minimum volume of ether and dried *in vacuo* (1·5 g.), m. p. *ca.* 150° (decomp.) (Found: C, 37·1; H, 4·1; As, 45·6; Fe, 8·8%; *M*, cryoscopic in 0·47% solution in benzene, 600. $C_{21}H_{32}OAs_4Fe$ requires C, 38·4; H, 4·8; As, 45·7; Fe, 8·5%; *M*, 656). The compound is soluble in all common organic solvents. Both in the solid state and in solution it is less stable than the previous monodiarsine substituted complex and is difficult to obtain very pure (this is reflected in the analyses). It is a poor conductor in nitrobenzene ($\Lambda_m = 2{\cdot}4$ mho in $1{\cdot}24 \times 10^{-3}$M-solution at 25°) and diamagnetic in powder form.

Monoiodomono-o-phenylenebisdimethylarsinedicarbonyliron(I).—Fresh $Fe(CO)_3$Diarsine (0·6 g.) in a cold dry mixture of benzene (50 ml.) and dry nitrobenzene (5 ml.) was treated slowly with iodine (0·18 g.) in cold, dry benzene (75 ml.) with constant stirring in an atmosphere of dry nitrogen. Care is necessary; a very slow addition favours decomposition of $Fe^0(CO)_3$Diarsine whilst a quick addition gives rise to large local concentrations of iodine favouring the higher (bivalent) oxidation state. Both factors may vitiate results. Light petroleum was added to the resulting solution; the compound (0·65 g.) was precipitated as a brownish-yellow microcrystalline powder and dried *in vacuo* (Found: C, 26·8; H, 3·11; I, 23·3; Fe, 10·55%; *M*, cryoscopic in 0·46% nitrobenzene solution, 410. $C_{12}H_{16}O_2As_2IFe$ requires C, 27·4; H, 3·05; I, 24·2; Fe, 10·66%; *M*, 525). The *compound* is fairly soluble in benzene and readily soluble in nitromethane and nitrobenzene. It is a very poor conductor in the latter ($\Lambda_m = 3{\cdot}6$ mho in $1{\cdot}36 \times 10^{-3}$M-solution at 25°). Magnetic susceptibility of the powder at 22·5° is $\chi_g = 2{\cdot}9 \times 10^{-6}$, $\chi_m = 1523 \times 10^{-6}$; diamagnetic correction 245×10^{-6}, whence $\mu_{eff.} = 2{\cdot}1$ B.M. The molecular weight is low, presumably owing to slight decomposition, an effect reflected in the conductivity also. A chloroform solution shows a peak in the visible region at 4300 Å and a shoulder in the ultraviolet at 3100 Å. On being heated the compound decomposes at *ca.* 195°.

Di-iodomono-o-phenylenebisdimethylarsinedicarbonyliron(II).—The monodiarsinetricarbonyl complex of iron, $Fe(CO)_3$Diarsine (0·6 g.) dissolved in dry ethyl ether (60 ml.) was treated with

[24] Nyholm and Parish, *Chem. and Ind.*, 1956, 470.

iodine (0·33 g.) in ether (40 ml.) in an inert and dry atmosphere with constant stirring. A dark brown shining microcrystalline precipitate was formed. The *compound* (0·8 g.) was filtered off under dry nitrogen and washed thoroughly with ether before being dried *in vacuo* (Found: C, 22·5; H, 2·65; I, 39·6; Fe, 8·8%; *M*, cryoscopic in 0·5% nitrobenzene solution, 624. $C_{13}H_{16}O_2As_2I_2Fe$ requires C, 22·0; H, 2·45; I, 39·0; Fe, 8·59%; *M*, 652). The substance, m. p. 186° (decomp.), dissolves readily in acetone or nitrobenzene, is moderately soluble in benzene, chloroform, and ethyl alcohol and sparingly soluble in absolute ether and insoluble in light petroleum or water. It is diamagnetic in powder form. In nitrobenzene the complex is virtually a non-electrolyte (Λ_m in $1·04 \times 10^{-3}$M-solution = 1·2 mho at 25°). A chloroform solution shows two peaks in the ultraviolet and visible spectrum at 3500 Å and 5000 Å respectively. Measurements could not be made further towards the ultraviolet region owing to heavy absorption by the diarsine.

Dibromomono-o-phenylenebisdimethylarsinedicarbonyliron(II).—$Fe(CO)_3$Diarsine (0·6 g.), in dry absolute ether (50 ml.), was treated with bromine (0·24 g.) in ether (35 ml.) in a dry nitrogen atmosphere with constant stirring. The orange-yellow crystals (0·79 g.), isolated as for the iodide, had m. p. 225° (decomp.) (Found: C, 25·5; H, 3·2; Br, 30·5; Fe, 10·1%; *M*, cryoscopic in 0·39% nitrobenzene solution, 508. $C_{12}H_{16}O_2As_2Br_2Fe$ requires C, 25·8; H, 2·9; Br, 28·7; Fe, 10·04%; *M*, 558). Solubilities are as for the iodide and it is diamagnetic. It is virtually a non-electrolyte in nitrobenzene, $\Lambda_M = 1·9$ mho in $1·24 \times 10^{-3}$M-solution at 25°. A chloroform solution shows peaks in the ultraviolet and visible spectrum at 3400 Å (shoulder) and 4800 Å.

Di-iodobis-o-phenylenebisdimethylarsineiron(II).—Bis-*o*-phenylenebisdimethylarsinemonocarbonyliron(0) (0·6 g.) in dry absolute ether (100 ml.) was treated with iodine (0·25 g.) in ether (50 ml.) with constant stirring. A brownish yellow precipitate was formed. This was filtered off, washed thoroughly with ether, and dried *in vacuo* (Found: C, 28·4; H, 4·2; I, 28·1; Fe, 6·3. $C_{20}H_{32}As_4I_2Fe$ requires C, 27·2; H, 3·7; I, 28·8; Fe, 6·33%). The *substance* is insoluble in all the common organic solvents and sparingly soluble in acetone or nitrobenzene. It could not be purified, although it is well characterised. An acetone solution of the compound gave no immediate precipitate of silver iodide on addition of silver nitrate solution, indicating that it is a non-electrolyte. The compound is diamagnetic in powder form. In Nujol, it shows no absorption peak in the C–O stretching-frequency range, indicating the absence of a carbonyl group.

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273. *Natural Occurrence of Enantiomorphous Leucoanthocyanidins: (+)-Mollisacacidin (Gleditsin) and Quebracho (−)-Leucofisetinidin.*

By J. W. Clark-Lewis and D. G. Roux.

The identity of gleditsin with mollisacacidin is confirmed and this dextrorotatory form of 7 : 3′ : 4′-trihydroxyflavan-3 : 4-diol is shown to be enantiomorphous with the (−)-leucofisetinidin from quebracho wood. Formation of *iso*propylidene derivatives from the leucofisetinidins indicates that they are *cis*-3 : 4-diols, and hydrogenation suggests that the 2-aryl and the 3-hydroxyl group are in *trans*-relation.

Few leucoanthocyanidins have been isolated from natural sources since King and Bottomley showed that the flavan-3 : 4-diol melacacidin [1] from *Acacia melanoxylon* (Australian blackwood) has leucoanthocyanidin properties. A flavan-3 : 4-diol structure [2]

[1] King and Bottomley, *Chem. and Ind.*, 1953, 1368; *J.*, 1954, 1399.
[2] Chan, Forsyth, and Hassall, *Chem. and Ind.*, 1957, 264; Forsyth, Hassall, and Roberts, *ibid.*, 1958, 656.

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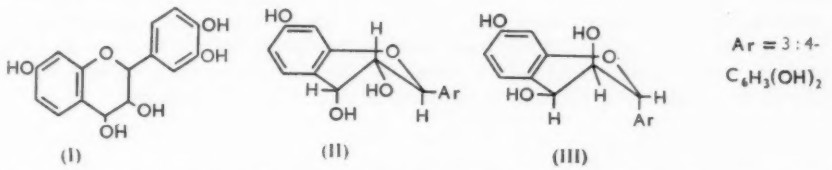
has been established for peltogynol but, apart from cacao-leucocyanidin,[3] leucodelphinidin,[4] and the flavandiols recently reported by Seshadri (see below), the only additions to the leucoanthocyanidin series are mollisacacidin [5] from *Acacia mollissima* (black wattle), gleditsin [6,7] from *Gleditsia* (*Gleditschia*) *japonica*, and the (—)-leucofisetinidin [8] from *Schinopsis quebracho-colorado*. These three compounds have the 7 : 3′ : 4′-trihydroxyflavan-3 : 4-diol structure (I), and the identity of the two dextrorotatory forms (mollisacacidin and gleditsin) [7] is now confirmed by comparing the trimethyl ethers, the trimethyl ether diacetates, and the trimethyl ether *iso*propylidene derivatives (m. p.s, mixed m. p.s, and absorption spectra).



(I) (II) (III)

(—)-Leucofisetinidin,[8] isolated from quebracho wood, resembled mollisacacidin closely, except in the sign of rotation, and the enantiomorphous nature of the two leucoanthocyanidins and their derivatives was established by their infrared absorption curves and by formation of racemates from equal quantities of (+)- and (—)-compounds. Moreover the melting points of the racemates were not depressed [9] by admixture with inactive derivatives prepared from natural fustin [10] or from synthetic *trans*-dihydro-7 : 3′ : 4′-trimethoxyflavonol.[11]

The enantiomorphism of (±)-mollisacacidin (gleditsin) and the (—)-leucofisetinidin from quebracho wood is thus unequivocally established, and these compounds are the first examples of enantiomorphous forms of a flavonoid in Nature. Further, either mollisacacidin (gleditsin) or the enantiomorphous (—)-leucofisetinidin must have the (2*S*)-configuration [12] and thus constitute an exception among optically active flavonoids which, hitherto, have been found to occur with the (2*R*)-configuration.[13,14] The stereochemistry of these leucofisetinidins can now be inferred, except for their absolute configurations. The formation of *iso*propylidene derivatives of these compounds is regarded as strong evidence for the *cis*-configuration of the 3 : 4-diol grouping, and supports the inference drawn from the formation of an acidic borate complex.[5] Moreover fustin, which yields racemic leucofisetinidin on hydrogenation,[10] is almost certainly a *trans*-compound like dihydroquercetin [14] and other naturally occurring dihydroflavonols.[15] Mollisacacidin (gleditsin) and quebracho (—)-leucofisetinidin may therefore be assigned the 2 : 3-*trans*-3 : 4-*cis*-configuration for which two half-chair conformations (II) and (III) are possible (also their mirror images). Assignment of the 2 : 3-*trans*-3 : 4-*cis*-configuration to the leucofisetinidins is supported by the work of Chandorkar and Kulkarni [11] who have prepared (±)-7 : 3′ : 4′-trimethoxyflavan-3 : 4-diol and its diacetate by reduction of synthetic *trans*-(±)-7 : 3′ : 4′-trimethoxydihydroflavonol with lithium aluminium hydride. The identity of these compounds with our racemates has been established by mixed m. p. determinations, and by

[3] Forsyth and Roberts, *Chem. and Ind.*, 1958, 755.
[4] Hathway, *Biochem. J.*, 1958, **70**, 34.
[5] Keppler, *Chem. and Ind.*, 1956, 380; *J.*, 1957, 2721.
[6] Mitsuno and Yoshizaki, *J. Pharm. Soc. Japan*, 1957, **77**, 557, 1208.
[7] Clark-Lewis and Mitsuno, *J.*, 1958, 1724.
[8] Roux, *Chem. and Ind.*, 1958, 161.
[9] Clark-Lewis and Roux, *ibid.*, p. 1475.
[10] Roux and Freudenberg, *Annalen*, 1958, **613**, 56.
[11] Chandorkar and Kulkarni, *Current Sci.*, 1957, **26**, 354.
[12] Cahn, Ingold, and Prelog, *Experientia*, 1956, **12**, 81.
[13] Birch, Clark-Lewis, and Robertson, *J.*, 1957, 3586; see, however, Brown and Somerfield, *Proc. Chem. Soc.*, 1958, 236.
[14] Clark-Lewis and Korytnyk, *J.*, 1958, 2367.
[15] Mahesh and Seshadri, *Proc. Indian Acad. Sci.*, 1955, **41**, *A*, 210; Whalley, "Chemistry of Vegetable Tannins," Soc. Leather Trades' Chemists, Croydon, 1956, p. 151.

infrared measurements on the diacetate. The closely related melacacidin (7 : 8 : 3′ : 4′-tetrahydroxyflavan-3 : 4-diol) probably has the 2 : 3-*cis*-3 : 4-*cis*-arrangement of substituents:[16] melacacidin resembles *epi*catechin in having the 2 : 3-*cis*-configuration and the leucofisetinidins resemble catechin in the 2 : 3-*trans*-configuration.

Robinson and Robinson[17] classified the leucoanthocyanidins into three groups according to solubilities; these probably correspond to (*a*) polymeric leucoanthocyanidins, *e.g.*, polymeric flavan-3 : 4-diols formed by condensation analogous to that proposed for catechins,[18] (*b*) leucoanthocyanidin glycosides (*i.e.*, leucoanthocyanins), and (*c*) monomeric leucoanthocyanidins, *e.g.*, flavan-3 : 4-diols. Progress so far has been restricted to group (*c*) and it is interesting that the monomeric flavan-3 : 4-diols first isolated all possessed hydroxyl groups in the 7- and the 4′-, but not the 5-position. Seshadri and his co-workers recently[19] isolated and characterised a leucopelargonidin, two leucocyanidins, and two leucodelphinidins from natural sources. Few details are yet available, but both leucodelphinidins evidently differ from the material described by Hathway.[4]

Experimental

Infrared absorptions were recorded with a Grubb–Parsons S4 spectrometer (for mulls and solutions) and with a Perkin–Elmer Infracord (for potassium bromide discs). $C_2H_2Cl_4$ below refers to 1 : 1 : 2 : 2-tetrachloroethane.

Materials.—Mollisacacidin obtained from *Acacia mollissima* heartwood and (−)-leucofisetinidin from *Schinopsis quebracho-colorado* sapwood were purified by preparative paper chromatography on thick sheets as already described.[20] The penta-acetates and the 7 : 3′ : 4′-trimethyl ethers and their diacetates were prepared as described for the (−)-leucofisetinidin derivatives.[20] Gleditsin and its derivatives were presented by Dr. M. Mitsuno. For mollisacacidin Keppler [5] reports $[\alpha]_D^{18}$ +12·6° (1% in MeOH) and we found $[\alpha]_D^{12}$ +31·4° (0·8% in 1 : 1 $COMe_2$–H_2O). For gleditsin we found $[\alpha]_D^{16}$ +14° (0·5% in MeOH) and Mitsuno and Yoshizaki [6] report $[\alpha]_D^{12}$ +33·6° (in 1 : 1 $COMe_2$–H_2O).

Mollisacacidin Trimethyl Ether.[5]—Crystallisation from aqueous ethanol gave the *sesquihydrate* in needles, sintering at 76—77° (cf. ref. 5), m. p. 91—94°, and 129° after resolidification, $[\alpha]_D^{16}$ −10·3° (1·12% in $C_2H_2Cl_4$) (Found: C, 59·9; H, 6·6; OMe, 26·4; loss on drying for 6 hr. at 70° *in vacuo*, 7·4. $C_{18}H_{20}O_6$,1·5H_2O requires C, 60·2; H, 6·45; OMe, 25·9; 1·5H_2O, 7·5%). Material dried for 5½ hr. at 60° *in vacuo* apparently lost only one molecule of water of crystallisation (Found: loss, 4·7. $C_{18}H_{20}O_6$,1·5H_2O requires 1H_2O, 5·0%).

Mollisacacidin trimethyl ether diacetate crystallised from ethanol in needles, m. p. 102°, $[\alpha]_D^{16}$ −17·1° (1·52% in $C_2H_2Cl_4$) (Found: C, 63·0; H, 5·8; OMe, 22·4; Ac, 19·8. $C_{22}H_{24}O_8$ requires C, 63·45; H, 5·8; OMe, 22·4; Ac, 20·7%). For the gleditsin derivative, Dr. Mitsuno [21] reports $[\alpha]_D^{10}$ −19·4° (2·8% in pyridine) and m. p. 100·5—101·5°.

Mollisacacidin 7 : 3′ : 4′-Trimethyl Ether iso*Propylidene Derivative.*—Mollisacacidin trimethyl ether was treated with acetone as described for (±)-melacacidin tetramethyl ether [16] and gave the iso*propylidene derivative* which crystallised from ethanol in prisms, m. p. 120—122°, $[\alpha]_D^{12}$ +5·8° (1·03% in $C_2H_2Cl_4$) (Found: C, 67·7; H, 6·55. $C_{21}H_{24}O_6$ requires C, 67·7; H, 6·50%). For the gleditsin derivative we found m. p. 117—118°.

(−)- *and* (±)-*Leucofisetinidin 7 : 3′ : 4′-Trimethyl Ether* iso*Propylidene Derivative.*—Quebracho (−)-leucofisetinidin trimethyl ether {m. p.s 81—84°, 134° (lit.,[22] 125—127°), $[\alpha]_D^{16}$ +9·4° (1·12% in $C_2H_2Cl_4$) (lit.,[22] $[\alpha]_D^{25}$ −3·8° (2% in $C_2H_2Cl_4$)} was converted into its iso*propylidene derivative* by the same method;[16] this crystallised from ethanol in prisms, m. p. 120—122°, $[\alpha]_D^{12}$ −6·3° (1·04% in $C_2H_2Cl_4$) (Found: C, 68·0; H, 6·4%).

[16] King and Clark-Lewis, *J.*, 1955, 3384.
[17] Robinson and Robinson, *J.*, 1935, 744.
[18] Freudenberg and Alonso, *Annalen*, 1958, **612**, 78.
[19] Seshadri and Laumas, *J. Sci. Ind. Res., India*, 1958, **17**, *B*, 44, 167; Seshadri and Ganguly, *ibid.*, p. 168.
[20] Roux and Evelyn, *Biochem. J.*, 1958, **70**, 334.
[21] Personal communication from Dr. Mitsuno.
[22] Freudenberg and Weinges, *Annalen*, 1958, **613**, 61.

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7 : 3′ : 4′-Trimethoxyflavan-3 : 4-diol, $[\alpha]_D^{15}$ −1·2° (0·82% in $C_2H_2Cl_4$), prepared by hydrogenation of fustin and subsequent methylation,[10] was similarly converted into the (±)-*isopropylidene derivative*, m. p. 134° (Found: C, 67·5; H, 6·5%). The product possessed slight optical activity, $[\alpha]_D^{15}$ −1·1° (0·94% in $C_2H_2Cl_4$).

Comparison of Mollisacacidin, Gleditsin, and (−)-Leucofisetinidin and their Derivatives.—(a) *The* 7 : 3′ : 4′-*trihydroxyflavan*-3 : 4-*diols*. Mollisacacidin, gleditsin, and quebracho (−)-leucofisetinidin all crystallised as dihydrates, in needles which melt with decomposition over a range. Mollisacacidin and gleditsin melted within the range 125—130°, alone or when mixed, when examined with a Leitz hot-stage microscope. A mixture of gleditsin and (−)-leucofisetinidin melted indefinitely in the range 127—146°.

Infrared spectra of mollisacacidin, gleditsin, and (−)-leucofisetinidin (Nujol mulls) were identical throughout the recorded range (2—15 μ). Mollisacacidin and (−)-leucofisetinidin (in KBr) gave identical curves which differed from that of the (±)-compound (prepared from fustin) as expected, although the curves were generally similar.

Paper chromatograms were sprayed with ammoniacal silver nitrate or 5% ethanolic toluene-*p*-sulphonic acid. The following R_F values were obtained for mollisacacidin, gleditsin, and (−)-leucofisetinidin, respectively: in BuOH–AcOH–H_2O (5 : 1 : 4), 0·62, 0·62, 0·62, in 2% AcOH, 0·58, 0·58, 0·52—0·53, in 2% AcOH (ascending), 0·50, 0·49, 0·46, and in Bu^sOH satd. with water, 0·76, —, 0·73.

(b) *Penta-acetates*. These have not yet been obtained crystalline and were unsuitable for detailed comparisons. Mollisacacidin penta-acetate, m. p. 82—87°, $[\alpha]_D^{15}$ −17·2° (1·02% in $C_2H_2Cl_4$), did not depress the m. p. of (−)-leucofisetinidin penta-acetate, m. p. 82—84°, $[\alpha]_D^{15}$ +16° (1·16% in $C_2H_2Cl_4$), and the mixture did not depress the m. p. of the (±)-penta-acetate, m. p. 82—84°, $[\alpha]_D^{15}$ −2·0° (1·49% in $C_2H_2Cl_4$), prepared from hydrogenated fustin. These amorphous materials did not melt sharply, and m. p.s here refer to the temperature of sintering and collapse. For gleditsin Dr. Mitsuno [21] reports m. p. 56—59°, $[\alpha]_D^{10}$ −7·5° (4·3% in pyridine).

(c) *Trimethyl ethers*. The m. p.s of the sesquihydrates were indefinite and appeared to depend upon the conditions (*e.g.*, rate of heating); after resolidification they had the same m. p.s as the anhydrous materials. Mollisacacidin trimethyl ether and gleditsin trimethyl ether behaved similarly, either alone or mixed together, when examined with the Leitz hot-stage microscope: m. p. 70—75° resolidification at *ca.* 100°, and m. p. 128—130° after sintering at 117—120° {cf. above; for the gleditsin ether Dr. Mitsuno [21] reports m. p. 130°, $[\alpha]_D^{10}$ +34·9° (4·5% in pyridine), and we found $[\alpha]_D^{16}$ −9·5% (0·5% in $C_2H_2Cl_4$}. A mixture of either compound with (−)-leucofisetinidin trimethyl ether similarly showed m. p. 65—70°, resolidification slowly at *ca.* 130° to a new crystalline form (racemate), m. p. 144—146°. The racemates prepared by evaporation of equimolar solutions of mollisacacidin (or gleditsin) trimethyl ether and quebracho (−)-leucofisetinidin trimethyl ether had m. p. 81—84°, resolidified at 120—130°, and then had m. p. 147—148° (in capillaries), alone or mixed with the trimethyl ether,[10] m. p. 149°, from hydrogenated fustin, and did not depress the m. p. of the (±)-7 : 3′ : 4′-trimethoxyflavan-3 : 4-diol,[11] m. p. 149°, supplied by Dr. Kulkarni (lit.,[11] m. p. 142°).

The infrared absorption of mollisacacidin, gleditsin, and quebracho (−)-leucofisetinidin trimethyl ethers in Nujol mulls and in chloroform were identical in the recorded ranges (2—15 and 2—11·5 μ). The curves from the chloroform solutions were identical with those of the two samples of racemate.[10,11] The infrared absorption curves of anhydrous mollisacacidin and gleditsin trimethyl ether were also identical (2—15 μ) when recorded with Nujol mulls of samples dried over phosphoric oxide at 110° *in vacuo*. The infrared spectra (in KBr) of mollisacacidin, (−)-leucofisetinidin, and the (±)-trimethyl ether [10] were indistinguishable.

(d) *Trimethyl ether* 3 : 4-*diacetates*. Mollisacacidin and quebracho (−)-leucofisetinidin trimethyl ether diacetate, $[\alpha]_D^{15}$ +16·5° (1·22% in $C_2H_2Cl_4$), had m. p. 101—102° and evaporation of an equimolar methanolic solution left a residue, m. p. 121—122° alone or mixed with the racemate supplied by Dr. A. B. Kulkarni [11] or that synthesised [10] from fustin. Infrared absorptions (in KBr) of the enantiomorphs were identical (2·5—15 μ), and closely similar to those of the two samples of racemate. The enantiomorphs (in Nujol mull) showed identical infrared absorptions (2—15 μ) which differed from that of the racemate; in carbon tetrachloride solution the enantiomorphs and the racemates [10,11] gave identical spectra (2—11·5 μ).

(e) *Trimethyl ether* iso*propylidene derivatives*. The mollisacacidin and the (−)-leucofisetinidin derivative, m. p. 120—122°, formed a racemate, m. p. 134° alone and when mixed

with the (±)-*iso*propylidene derivative described above. The infrared curves of the enantiomorphs (in KBr) were indistinguishable and closely similar to that recorded for the racemate.

We recorded also the following data. Quebracho leucofisetinidin, m. p. 130° (decomp.) (lit.,[22] 133—137°), $[\alpha]_D^{25}$ −11·1° in MeOH [lit.,[22] −12° (2%)], $[\alpha]_D^{18}$ −31·7° (0·8% in 1 : 1 acetone–water) {lit.,[22] $[\alpha]_D^{25}$ −32° (2%)}. (±)-Leucofisetinidin [ref. 10 gives m. p. 126—130° (decomp.) (dried over P_2O_5)], $[\alpha]_D^{15}$ −2·2° (0·82% in 1 : 1 acetone–water) {lit.,[10] $[\alpha]_D^{21}$ −2·4° (1·4%)}; its trimethyl ether, $[\alpha]_D^{15}$ −1·2° (0·82% in $C_2H_2Cl_4$); its trimethyl ether diacetate, m. p. 121—122° (lit., 121—122°,[10] and 122° [11]), $[\alpha]_D^{15}$ +1·2° (1·24% in $C_2H_2Cl_4$).

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274. *The Alkaloids of the Roots of* Datura.

By W. C. Evans and M. Wellendorf.

3α-Tigloyloxytropane, hitherto not recorded as a natural product, has been obtained from the roots of *Datura ferox*. Tigloidine, atropine, tropine, *pseudo*tropine, and an uncharacterised base have been isolated from the roots of *D. innoxia*. The roots of both species contain 7-hydroxy-3 : 6-ditigloyloxytropane, (−)-3α : 6β-ditigloyloxytropane, hyoscine, and meteloidine.

The complex nature of the alkaloid mixture contained in the roots of *Datura* species was shown by application of partition chromatography to the separation of tropane alkaloids.[1] Since then paper chromatography has detected hyoscine, hyoscyamine, and cuscohygrine in the roots of *D. ferox* L.[2,3] and *D. innoxia* Miller and meteloidine [2] in the former. Other bases, the constitutions of which have not been fully elucidated, have been reported in both species.[4,5] 7-Hydroxy-3 : 6-ditigloyloxytropane [6] has been isolated from extracts of the roots of *D. ferox* and (−)-3α : 6β-ditigloyloxytropane [7] from those of *D. innoxia*; the results of the continued investigation of these, and similar extracts, are recorded here.

An ether extract of the roots of *D. ferox* was resolved into six fractions by partition chromatography, light petroleum (b. p. 60—80°), ether, and chloroform being used successively as eluants. Repeated chromatography of the first fraction afforded 3α : 6β-ditigloyloxytropane together with the 7-hydroxy-derivative. The ether eluate contained first hyoscine and then 3α-tigloyloxytropane, which was recovered from the titration liquors as the picrate identical with that of the ester prepared from tropine and tigloyl chloride according to the method of Barger, Martin, and Mitchell.[8] We were unable, however, to obtain 3α-tigloyloxytropane picrate with the m. p. ascribed to it by these workers although the properties of the hydrobromides were identical. The first fractions of the chloroform eluate contained meteloidine and the later ones two other bases which have not been characterised but which, by paper chromatography, appear to be alkamines. No evidence for the presence of hyoscyamine in these roots was obtained.

[1] Evans and Partridge, *Quart. J. Pharm.*, 1948, **21**, 126.
[2] Romeike, *Flora*, 1956, **143**, 67.
[3] Reinouts van Haga, *Nature*, 1954, **174**, 833.
[4] Steinegger and Gessler, *Pharm. Acta Helv.*, 1955, **30**, 279.
[5] Romeike and Zimmermann, *Naturwiss.*, 1958, **45**, 187.
[6] Evans and Partridge, *J.*, 1957, 1102.
[7] Evans and Wellendorf, *J.*, 1958, 1991.
[8] Barger, Martin, and Mitchell, *J.*, 1937, 1820.

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From a slightly acid solution of the total alkaloids of *D. innoxia* roots in sulphuric acid, 7-hydroxy-3 : 6-ditigloyloxytropane, together with the small amount of 3α : 6β-ditigloyloxytropane already reported,[7] was collected in chloroform. To portions of the aqueous solutions, aliquot portions of alkali were added, and the fractionally-liberated bases successively removed in chloroform (Fractions A2—A12). Fraction A2 consisted almost entirely of 7-hydroxy-3 : 6-ditigloyloxytropane and fraction A3 afforded tigloidine (3β-tigloyloxytropane) together with hyoscine, meteloidine, atropine, and small quantities of a base previously reported in the leaves of *D. ferox*.[8] The optical rotation of the isolated hyoscine and the m. p. of its salts indicated a mixture of the (−)- and the (±)-form. Fractions A8 to A12 contained a mixture of tropine and *pseudo*tropine and these bases were separated for characterisation by the esterification of the mixture with tigloyl chloride followed by chromatographic fractionation of the mixed esters.

The proportions (%) of the principal alkaloids in samples of these roots are given in the Table.

Root	(I)	(II)	(III)	(IV)	(V)
D. innoxia (Pakistan sample)	0·02	0·11	0·19	0·15	0·02
D. innoxia (English sample)	0·08	0·19	0·22	0·25	0·06
D. innoxia (English, Texas seeds)	0·03	0·12	0·27	0·31	0·06
D. ferox (English, Australian seeds)	0·01	0·03	0·03	0·05 *	0·004

(I), 3α : 6β-Ditigloyloxytropane. (II), 7-Hydroxy-3 : 6-ditigloyloxytropane. (III), Hyoscine. (IV), Atropine and meteloidine (as meteloidine). (V), Tropine and *pseudo*tropine.

* Meteloidine only.

The two ditigloyl esters appear to be constant constituents of the roots of *Datura* species, both alkaloids having also been isolated from *D. stramonium*.[6,7] The occurrence of tigloidine, not previously reported in this genus, forms another phytochemical link with the genus *Duboisia*. Racemised hyoscine and hyoscyamine, together with alkamines of the tropane esters, appear to be chiefly confined to the roots of *Datura* spp.; with the aerial organs of the plants they are usually found only in poorly dried and stored material.

Experimental

The Alkaloids of the Roots of D. ferox.—The chromatographic column from which light petroleum (b. p. 60—80°) had removed 7-hydroxy-3 : 6-ditigloyloxytropane [6] was developed with ether and aliquot portions of the eluate were titrated with 0·02N-sulphuric acid; this gave three more bands. From the first, equivalent to 0·04 g. of hyoscine, crystalline products could not be obtained; the second afforded hyoscine (0·15 g.) [aurichloride, m. p. and mixed m. p. 209° (Found: C, 31·9; H, 3·7; Au, 30·9. Calc. for $C_{17}H_{21}O_4N,HAuCl_4$: C, 31·7; H, 3·4; Au, 30·6%)]. The third ether fraction was eluted as a wide homogeneous band and the aqueous titration liquors, made alkaline with ammonia solution, were shaken with chloroform; separation and removal of solvent left a gum (0·05 g.) which, neutralised with dilute sulphuric acid and treated with sodium picrate, gave 3α-*tigloyloxytropane picrate* (from aqueous alcohol), m. p. 180° (Found: C, 50·7; H, 5·5; N, 12·5. $C_{13}H_{21}O_2N,C_6H_3O_7N_3$ requires C, 50·4; H, 5·3; N, 12·4%). Chloroform was then used to elute two more bands from the column. The base isolated from the first was transferred to a column of kieselguhr (40 g.) loaded with 0·5M-phosphate buffer (40 ml.; pH 7·2), and eluted with ether. The recovered base (0·52 g.), in neutral solution, with sodium picrate afforded meteloidine picrate, m. p. and mixed m. p. 178° (Found: C, 47·4; H, 5·0; N, 11·9. Calc. for $C_{13}H_{21}O_4N,C_6H_3O_7N_3$: C, 47·1; H, 4·9; N, 11·6%). Paper chromatography of the second chloroform fraction indicated two alkamines having approximately the same R_F value as tropine and giving a similar purple colour when chromatograms of it were sprayed with modified Dragendorff's reagent.

For the isolation of 3α : 6β-ditigloyloxytropane, the powdered root (225 g.) was moistened with water (60 ml.) and kept for 2 hr. Calcium hydroxide (20 g.) was mixed in and the powder exhaustively extracted with ether. The percolate was evaporated to dryness and the green residue transferred to kieselguhr (20 g.) loaded with 0·5M-phosphate buffer (12 ml.; pH 6·6). The first fraction eluted with light petroleum (b. p. 60—80°), which previous observations had indicated as homogeneous,[6] was resubmitted to partition chromatography on kieselguhr (20 g.)

and 0·5M-phosphate buffer (12·0 ml.; pH 6·0). Elution of the chromatogram with light petroleum afforded two fractions. The base (0·014 g.) recovered from the first was neutralised with dilute sulphuric acid and on treatment with sodium picrate furnished 3α : 6β-ditigloyloxytropane picrate, m. p. and mixed m. p. 150° (Found: C, 52·2; H, 5·7. Calc. for $C_{18}H_{27}O_4N,C_6H_3O_7N_3$: C, 52·4; H, 5·5%). The alkaloid (0·077 g.) from the second fraction was neutralised with alcoholic hydrobromic acid; addition of ether to the solution precipitated 7-hydroxy-3 : 6-ditigloyloxytropane hydrobromide, m. p. and mixed m. p. 215° (Found: C, 51·5; H, 6·6. Calc. for $C_{18}H_{27}O_5N,HBr$: C, 51·7; H, 6·7%).

The Alkaloids of the Roots of D. innoxia.—An extract of Pakistan root (32 kg.) containing an equivalent of 128 g. of hyoscyamine was obtained in a faintly acid [sulphuric acid] solution and repeatedly shaken with chloroform.[7] Eleven other chloroform solutions of alkaloids of increasing basicity were similarly obtained by the successive addition of aliquot portions (usually 30 ml.) of N-sodium hydroxide to a portion of the solution. Removal of the solvent gave fractions A1—A12. The interaction of sodium picrate and a neutral solution of fraction A1 (0·5 g.) afforded, after repeated recrystallisation from aqueous alcohol, a picrate as prisms, m. p. 173—173·5° (Found: C, 52·2; H, 5·5%). From the original mother liquor of this picrate, the isolation of 3α : 6β-ditigloyloxytropane picrate has already been recorded.[7] The infrared spectrum of the picrate, m. p. 173—173·5°, compared with that of 7-hydroxy-3 : 6-ditigloyloxytropane picrate showed reduced bands at 1695, 1557, 1107, 1020, and 745 cm.$^{-1}$ together with a partial disappearance of the doublet at 1073 and 1183 cm.$^{-1}$ and a corresponding tendency towards the single band of 3α : 6β-ditigloyloxytropane picrate at 1077 cm.$^{-1}$. The picrate (0·28 g.) in chloroform (40 ml.) was washed with successive quantities (40 ml.) of aqueous ammonia until the chloroform solution was colourless. Removal of the solvent left a gum, $[\alpha]_D^{20}$ −3·6° (*c* 7·9 in ethanol, *l* 5 cm.), which was transferred to kieselguhr (20 g.) loaded with 0·5M-phosphate buffer (12·4 ml.; pH 6·0). The petroleum eluate was collected in two fractions the first of which furnished 3α : 6β-ditigloyloxytropane (0·024 g.), $[\alpha]_D^{20}$ −18·7° (*c* 7·9 in ethanol, *l* 5 cm.), which in neutral solution with dilute sodium picrate afforded the picrate, m. p. and mixed m. p. 150—151° (Found: C, 52·4; H, 5·4%). The second fraction gave 7-hydroxy-3 : 6-ditigloyloxytropane [α = 0°; picrate, m. p. and mixed m. p. 180·5° (Found: C, 51·3; H, 5·4. Calc. for $C_{18}H_{27}O_5N,C_6H_3O_7N_3$: C, 50·9; H, 5·3; N, 9·9%)].

A neutral solution of fraction A2 in dilute hydrobromic acid deposited 7-hydroxy-3 : 6-ditigloyloxytropane hydrobromide, m. p. and mixed m. p. 214—215°, from which the picrate, m. p. and mixed m. p. 181° (Found: C, 50·9; H, 5·3; N, 9·9%), was prepared.

Paper chromatograms showed fraction A3 (4·5 g.) to contain a mixture of bases, principally of intermediate R_F values. The fraction was obtained in neutral solution with dilute sulphuric acid, and the alkaloids were fractionally liberated by the addition of ten aliquot parts (20 ml.) of 0·1N-sodium hydroxide and successively collected in chloroform. Removal of the solvent gave fractions B1—B10 of which B5 to B8 were further fractionated by chromatography on kieselguhr (20 g.) loaded with 0·5M-phosphate buffer (10 ml.; pH 6·6). The petroleum fraction, which paper chromatography indicated to be homogeneous, afforded a base (0·04 g.) that with dilute hydrobromic acid deposited tigloidine hydrobromide, m. p. and mixed m. p. 232·5° (Found: C, 51·3; H, 7·1. Calc. for $C_{13}H_{21}O_2N,HBr$: C, 51·3; H, 7·2%). From the hydrobromide, tigloidine picrate was prepared, m. p. and mixed m. p. 240° (Found: C, 50·7; H, 5·5%). Continued elution of the column with ether afforded two bases: hyoscine (1·2 g.), $[\alpha]_D^{20}$ −7·4° (*c* 3·8 in water, *l* 5 cm.), characterised as the hydrobromide, m. p. 182° (softening 172°) (Found: C, 52·8; H, 5·5. Calc. for $C_{17}H_{21}O_4N,HBr$: C, 53·1; H, 5·7%), and the picrate m. p. finally 192° (softened 178°). A minor component (0·015 g.) of the ether eluate afforded a picrate, prisms from aqueous alcohol, m. p. 230° undepressed on admixture with the picrate of the alkaloid of identical R_F value obtained from the leaves of *D. ferox*.[9] Finally chloroform was used to elute meteloidine (0·173 g.) from which the picrate, m. p. and mixed m. p. 176—177° (Found: C, 47·1; H, 4·9; N, 11·4%), was prepared. Paper chromatograms showed fractions B9 and B10 to contain bases with R_F values identical with those of meteloidine and atropine. The basic mixture (0·3 g.) in neutral solution (with dilute sulphuric acid) on treatment with sodium picrate gave atropine picrate (0·2 g.), m. p. and mixed m. p. 173—174° (Found: C, 53·4; H, 5·2. Calc. for $C_{17}H_{23}O_3N,C_6H_3O_7N_3$: C, 53·3; H, 5·0%).

Paper chromatograms of samples of fractions A8—A11, sprayed with modified Dragendorff's reagent, indicated the presence of two bases of low R_F value; one gave a purplish, and the

[9] Evans and Partridge, *J. Pharm. Pharmacol.*, 1949, **1**, 593.

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other an orange stain with the reagent. A neutral solution of a portion (0·06 g.) of these fractions (with sulphuric acid) gave with sodium picrate, tropine picrate (0·07 g.), m. p. and mixed m. p. 274° (decomp.) (Found: C, 45·8; H, 5·3; N, 15·3. Calc. for $C_8H_{15}ON,C_6H_3O_7N_3$: C, 45·4; H, 4·9; N, 15·1%). Another portion (0·38 g.) and tigloyl chloride (0·4 g.) were kept at 105° for 3 hr.; the unchanged acid chloride was then decomposed by warming the mixture with water, and tiglic acid removed with ether. The esterified bases were collected in chloroform. Removal of the solvent gave a gum (0·41 g.) which was transferred in ether on to kieselguhr (20 g.) loaded with 0·5M-phosphate buffer (12·8 ml.; pH 6·0). Two alkaloids were obtained by elution of the chromatogram with ether. The weaker base (0·07 g.) in neutral solution yielded tigloidine picrate, m. p. and mixed m. p. 237° (Found: C, 50·3; H 5·2%). The stronger base was obtained as a gum (0·28 g.) which in neutral solution in alcoholic hydrobromic acid deposited, after concentration of the solution, 3α-tigloyloxytropane hydrobromide, m. p. and mixed m. p. 206·5° (Found: C, 51·1; H, 7·0%). The addition of sodium picrate to the aqueous hydrobromide afforded the picrate, m. p. and mixed m. p. 180° (Found: C, 50·4; H, 5·4; N, 12·5%).

3α-Tigloyloxytropane Hydrobromide and Picrate.—These compounds were prepared by the method of Barger *et al.*[8] from tropine (0·03 g.) obtained by hydrolysis of atropine. The ester was purified by chromatography, kieselguhr (15 g.) and 0·25M-phosphate buffer (10 ml.; pH, 6·0) being employed. The chromatogram was washed with ether, and then the tigloyloxytropane (0·05 g., 95%) removed in ether–chloroform (1 : 1 v/v). The properties of the hydrobromide were those ascribed to it by Barger *et al.* but the picrate, m. p. 180° (Found: C, 50·1; H, 5·3; N, 11·9%), prepared from it could not be obtained with m. p. 200°.[8]

Quantitative Determination of the Principal Alkaloids of Datura *Roots.*—The powdered roots (3 or 5 g.) were assayed by Evans and Partridge's method [10] except that carbon tetrachloride was replaced by light petroleum which was collected in aliquot parts (7·5 ml.) and each titrated to give an estimate of the 3α : 6β-ditigloyloxytropane and 7-hydroxy-3 : 6-ditigloyloxytropane content. The ether fraction corresponded to hyoscine, the chloroform eluate to the total meteloidine and atropine and, the final ammoniacal chloroform eluate contained the tropine-*pseudo*tropine mixture. The homogeneity of the fractions was checked by paper chromatography.

We thank Professor N. A. Qazilbash, Peshawar, for arranging collection of the Pakistan roots.

THE DEPARTMENT OF PHARMACY, UNIVERSITY OF NOTTINGHAM. [*Received, October 9th,* 1958.]

[10] Evans and Partridge, *J. Pharm. Pharmacol.*, 1952, **4**, 769.

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275. *The Synthesis of* 8-*Phenyl*meso*benzanthrone.*

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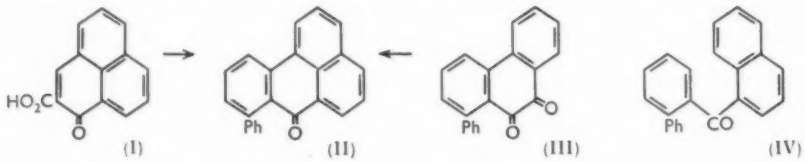
Two syntheses of 8-phenyl*meso*benzanthrone are described.

FEW 8-substituted *meso*benzanthrones have been reported, partly because efforts to synthesise them have been nullified by the attendant isomerisation under the action of aluminium chloride.[1] We have synthesised 8-phenyl*meso*benzanthrone by two methods without using aluminium chloride, but neither method is of preparative value. 1-Oxoperinaphthene-2-carboxylic acid (I) condensed with phenylbutadiene to give a product which is either 8- or 11-phenyl*meso*benzanthrone.[2] It was proved to be the former (II) since it was identical with the substance obtained by heating 1-phenylphenanthraquinone (III) with sulphuric acid, ferrous sulphate, and glycerol.[3] The ultraviolet spectrum of 8-phenyl*meso*benzanthrone closely resembles those of *meso*benzanthrone and 3- and 6-phenyl-*meso*benzanthrone,[4] and differs from that of 2-phenyl*meso*benzanthrone (see Figure).

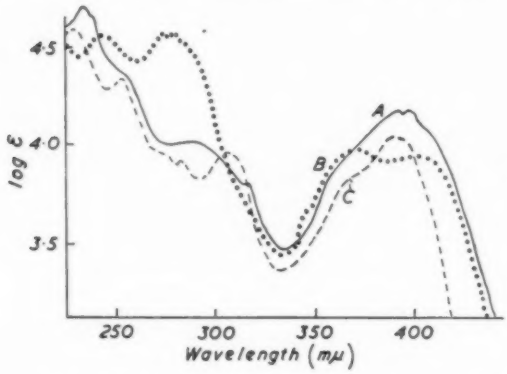
[1] Mayer, Fleckenstein, and Gunther, *Ber.*, 1930, **63**, 1466.
[2] Cf. Fieser and Newton, *J. Amer. Chem. Soc.*, 1942, **64**, 920.
[3] Turski and Pragierowa, *Przemysl Chem.*, 1929, **13**, 33; *Chem. Abs.*, 1929, **23**, 1899.
[4] Clar and Stewart, *J. Amer. Chem. Soc.*, 1952, **74**, 6235; Hartmann and Lorenz, *Z. Naturforsch.*, 1952, **7a**, 360.

This absence of interaction between the phenyl and the *meso*benzanthrone residues in the 3-, 6-, and 8-phenyl compounds is similar to that encountered in the 1-arylnaphthalenes and in the 1-aryl- and 1 : 5- and 1 : 8-diaryl-anthraquinones and is attributed to steric inhibition of planarity of the aryl groups with the rest of the molecule.[5]



Attempts to convert 1-phenylanthraquinone into phenyl*meso*benzanthrones by heating it with glycerol and sulphuric acid were unsuccessful owing to sulphonation of the phenyl nucleus.

Heating 1-*o*-phenylbenzoylnaphthalene (IV) with aluminium chloride gave a mixture from which only *meso*benzanthrone in very small quantity was isolated. The same



Ultraviolet absorption spectra of (*A*) 8-*phenyl*-meso*benzanthrone*, (*B*) 2-*phenyl*meso-*benzanthrone, and* (*C*) meso*benzanthrone*.

method with 1-*p*-phenylbenzoylnaphthalene yielded 10-phenyl*meso*benzanthrone, confirming the results of previous workers,[6] but there was evidence that other products had been formed.

The preparation of 1-*o*-phenylbenzoylnaphthalene (IV) presented some points of interest. Methyl *o*-phenylbenzoate and excess of 1-naphthylmagnesium bromide gave 2-diphenylyl-1-naphthylmethanol (IV; CO replaced by CH·OH) whose spectrum resembled that of α-1-naphthylbenzyl alcohol. Presumably the ketone first formed was reduced by the Grignard reagent since it is known that 1-benzoylnaphthalene is reduced in this way to the alcohol.[7]

o-Phenylbenzoyl chloride and naphthalene in the presence of aluminium chloride yielded fluorenone and indeed the mere distillation of the acid chloride in the absence of catalyst yielded the same product. 1-Naphthonitrile and 2-diphenylylmagnesium iodide, however, afforded 1-*o*-phenylbenzoylnaphthalene (IV), which formed a dinitrophenylhydrazone and whose ultraviolet spectrum resembled that of 1-benzoylnaphthalene. Attempts to reduce the ketone with lithium aluminium hydride and with potassium borohydride were unsuccessful and the Meerwein–Ponndorf method somewhat unexpectedly yielded mainly 1-2′-phenylbenzylnaphthalene (IV; CH_2 for CO) although similar reductions

[5] Braude, Fawcett, and Webb, *J.*, 1954, 1049; Friedel, Orchin, and Reggel, *J. Amer. Chem. Soc.*, 1948, **70**, 199.
[6] Scholl and Seer, *Annalen*, 1912, **394**, 148; Schmidlin and Garcia-Banus, *Ber.*, 1912, **45**, 3183.
[7] Blicke and Powers, *J. Amer. Chem. Soc.*, 1929, **51**, 3378; Davies, Dixon, and Jones, *J.*, 1930, 1916.

to a methylene group have occasionally been reported.[8] The benzyl compound was also prepared by dehydrogenating 1 : 2-dihydro-4-2′-phenylbenzylnaphthalene, and (along with other products) by the interaction of 2-phenylbenzyl bromide and naphthalene in carbon disulphide in the presence of aluminium chloride.

Experimental

M. p.s were determined on a Kofler block; chromatographic separations were effected on alumina; and fluorescence observations were made under a Hanovia ultraviolet lamp.

Syntheses of 8-*Phenyl*meso*benzanthrone.*—(*a*) 1-Oxoperinaphthene-2-carboxylic acid (1 g.) was boiled (19 hr.) with 1-phenylbuta-1 : 3-diene (6 ml.) in acetic acid (40 ml.). The residue obtained after steam-distillation of the mixture was dissolved in ether–benzene, dried (Na_2SO_4), and evaporated to dryness. The residue in benzene was chromatographed on a column 14″ × ¾″ and was developed with benzene. A yellow zone with a dull yellow fluorescence yielded on elution and evaporation 8-*phenyl*meso*benzanthrone* (22%), yellow needles (from benzene or ethanol–acetic acid), m. p. 201—202° (Found: C, 90·2; H, 4·6. $C_{23}H_{14}O$ requires C, 90·2; H, 4·6%), $\lambda_{max.}$ (log ε in parentheses), 233 (4·64), 288 (3·98), 318 (3·76), 395 mμ (4·12), giving in concentrated sulphuric acid a dark red solution with an orange fluorescence even in daylight.

(*b*) 1 : 2 : 3 : 4-Tetrahydro-1-oxophenanthrene was obtained in 85% yield by the ring-closure of 4-1′-naphthylbutanoic acid with polyphosphoric acid (12 g. of phosphoric oxide and 10 ml. of phosphoric acid per g. of acid) and was converted into 1-phenylphenanthrene. Oxidation with chromic anhydride and acetic acid yielded 1-phenylphenanthraquinone, orange plates (3·8 g.), m. p. 229—230°, after two crystallisations from ethanol, and identical with a sample prepared by another method.[9]

The quinone (0·47 g.) in concentrated sulphuric acid (15 c.c.) was added to ferrous sulphate heptahydrate (9·0 g.) and glycerol (1·0 g.) in water (10 c.c.) and heated at 100° (1 hr.) and then 150—160° (1 hr.). The mixture was poured into water (100 c.c.) and kept for 3 hr., and the precipitate filtered off and washed with water. The residue was extracted with chloroform (24 hr.), and the solvent evaporated. The residue in benzene was chromatographed on a column 8″ × ½″. Development with benzene yielded a bright yellow zone which on elution with benzene gave 8-phenyl*meso*benzanthrone, yellow needles (20 mg.) (after two crystallisations from ethanol), m. p. 198°, undepressed when mixed with a sample prepared by the first method.

Ring-closure of 1-o-*Phenylbenzoylnaphthalene.*—The ketone (500 mg.), aluminium chloride (2 g.), and sodium chloride (750 mg.) were fused for 1 hr. in an oil-bath at 120—130°. Decomposition of the cooled mass by ice and hydrochloric acid gave a precipitate, which was washed with dilute hydrochloric acid and water, and boiled with acetic acid. The acetic acid on evaporation gave a residue which in benzene was chromatographed on a column 4 × ¼″. The main yellow zone, on elution, yielded an orange solid (15 mg.), which after crystallisation (twice) from methanol gave yellow needles, m. p. 171—173°, undepressed when mixed with *meso*benzanthrone, m. p. 171°, but there was evidence that the compound was not pure.

Ring-closure of 1-p-*Phenylbenzoylnaphthalene.*—Cyclisation was performed as described above, and somewhat impure 10-phenyl*meso*benzanthrone (60 mg.), yellow needles, m. p. 169—171° (lit., 170—171°, 174—175°), was obtained after chromatography and crystallisation from acetic acid and from 80% methanol. A big m. p. depression was obtained when the product was mixed with *meso*benzanthrone.

Preparation of 2-*Diphenylyl*-1-*naphthylmethanol.*—Methyl diphenyl-2-carboxylate (10 g.) in anhydrous benzene was added to the Grignard reagent prepared from 1-bromonaphthalene (37·2 g.), magnesium (4·4 g.), anhydrous ether (100 c.c.), and benzene (25 c.c.). The mixture was distilled until the distillation temperature reached 55°. It was then boiled for 18 hr. and poured into hydrochloric acid and ice. The two layers were separated and the aqueous layer was extracted with benzene. The organic layers were combined and steam-distilled. The residual oil was dissolved in a boiling mixture of acetic acid and ethanol. The cooled solution deposited 2-*diphenylyl*-1-*naphthylmethanol* (70%), pale yellow prisms (after two crystallisations from acetic acid), m. p. 154—155° (Found: C, 89·2; H, 5·5. $C_{23}H_{18}O$ requires C, 89·0; H,

[8] Campbell and Woodham, *J.*, 1952, 843; Coffey and Boyd, *J.*, 1954, 2468.
[9] Leaver, unpublished results; Fuson and Tomboulian, *J. Amer. Chem. Soc.*, 1957, **79**, 956.

5·9%). The substance in concentrated sulphuric acid gives a violet solution with a blue fluorescence.

Preparation of 1-o-*Phenylbenzoylnaphthalene.*—1-Naphthonitrile (6·5 g.) in anhydrous benzene (75 c.c.) was added to the Grignard reagent made from 2-iododiphenyl (16·5 g.), magnesium (1·65 g.), and anhydrous ether (165 c.c.). Solvent (50 c.c.) was distilled from the solution, and the remaining solution boiled for 14 hr. To the mixture were added dropwise water (20 c.c.) and then concentrated hydrochloric acid (20 c.c.). The solvent were removed in a vacuum, glacial acetic acid (10 ml.) was added, and the mixture heated for 1 hr. on the water-bath. The mixture was steam-distilled until no more oil appeared in the distillate and the residue, which solidified on cooling, was dissolved in hot acetic acid (150 ml.), and the red solution slowly cooled. 1-o-*Phenylbenzoylnaphthalene* (66%) separated; it formed yellow prisms (from ethanol), m. p. 130° (Found: C, 89·5; H, 5·4. $C_{23}H_{16}O$ required C, 89·6; H, 5·2%). The substance gives a red solution showing a yellow fluorescence in sulphuric acid and forms by Brady's method (with the boiling extended to 14 hr.) a dinitrophenylhydrazone, dark red prisms, m. p. 216—220°, which was not obtained pure (Found: N, 10·6. Calc. for $C_{29}H_{20}O_4N_4$: N, 11·5%).

1-2′-*Phenylbenzylnaphthalene.*—The above ketone (1·0 g.) was boiled for 1 hr. with aluminium *iso*propoxide prepared from aluminium (0·5 g.) in anhydrous propanol-2-ol. The condenser was replaced by a Hahn partial-reflux condenser with methanol as cooling agent. After 2 hr. no more acetone came over and the mixture was boiled under a full-reflux condenser for 14 hr. Removal of the solvent gave a residue which was decomposed with 4N-sulphuric acid and ice, and the resultant oil was extracted with ether. The dried (Na_2SO_4) ether solution was evaporated in a vacuum, and gave impure 1-2′-phenylbenzylnaphthalene, colourless needles (0·5 g.) (from ethanol), m. p. *ca.* 96° (Found: C, 94·3; H, 5·7. $C_{23}H_{18}$ requires C, 93·8; H, 6·2%).

Ethyl diphenyl-2-carboxylate (6 g.) in ether (100 ml.) was added to lithium aluminium hydride (1 g.) in ether (75 ml.), stirred for ¾ hr., boiled for ½ hr., kept overnight, and after the usual procedure yielded 2-*phenylbenzyl alcohol* (80%), b. p. 179—180°/9 mm., m. p. 41—42° (Found: C, 86·2; H, 6·5. $C_{13}H_{12}O$ requires C, 84·8; H, 6·6%). The alcohol (87%) was also obtained by a similar reduction of *o*-phenylbenzoic acid. 2-Phenylbenzyl bromide (5 g.) (from the alcohol and hydrobromic acid) in ether (100 ml.) was added to magnesium (0·5 g.) in ether (40 ml.) at 0—5°, and to the stirred Grignard reagent 1-tetralone (3 g.) in ether (40 ml.) was added at 0—5°. Decomposition with ice and hydrochloric acid gave an oil, which when cooled in carbon dioxide–acetone afforded crystalline 1 : 2-*dihydro*-4-2′-*phenylbenzylnaphthalene*, needles (from light petroleum), m. p. 112—112·5° (Found: C, 92·5; H, 6·6. $C_{23}H_{20}$ requires C, 93·2; H, 6·8%). It gives an orange colour in sulphuric acid. Dehydrogenation with palladised charcoal in an atmosphere of carbon dioxide yielded 1-2′-*phenylbenzylnaphthalene*, needles (from acetic acid), m. p. 121—122° with sublimation (Found: C, 93·7; H, 6·2. $C_{23}H_{18}$ requires C, 93·8; H, 6·2%). This compound (50 mg.) was also obtained by keeping naphthalene (3·5 g.), 2-phenylbenzyl bromide (3 g.), and stannic chloride (2 g.) in carbon disulphide (18 ml.) for 2 days and boiling (6 hr.), followed by decomposition with ice and hydrochloric acid.

Spectroscopic Measurements.—The ultraviolet spectra of the following substances were measured by means of a Unicam S.P. 500 quartz spectrophotometer. The solvent was 95% ethanol and log ε is given in parentheses. 2-Phenyl*meso*benzanthrone: 243, 275, 370, 403 mμ (4·53, 4·54, 3·95, and 3·92). 3-Phenyl*meso*benzanthrone: 230, 290, 305, 407 mμ (4·58, 4·12, 4·03, 4·15). 6-Phenyl*meso*benzanthrone: 232, 258, 283, 324, 395 mμ (4·56, 4·43, 4·12, 3·79, and 3·94).

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276. *The Optical Rotatory Dispersion of Hydrocarbons. (+)-3-Methylhexane.*

By B. C. Easton and M. K. Hargreaves.

The effect of certain solvents on the optical rotatory dispersion of (+)-3-methylhexane is recorded. The rotatory powers in these solvents depend on the refractive index in an unusual manner.

The synthesis of 3-methylhexane *via* pentyl-lithium has some advantage over previous methods.

The rotatory powers of 3-methylheptane show quite large variations with solvent.[1] The rotatory dispersion of the simplest optically active paraffin, 3-methylhexane, is similar to that of its homologue. Thus there is a considerable reduction in the optical rotatory power on dissolution in carbon disulphide; this is accompanied by a change in the dispersion ratio $[\alpha]_{4358}/[\alpha]_{5461}$. This change is, however, small when compared with that shown by other substances on change of solvent.[2] These variations are of interest because they cannot be ascribed to interaction or bonding of any appreciable strength. A minor interaction due to polarity at the tertiary hydrogen position is possible but seems unlikely.

Changes in rotatory power and rotatory dispersion with solvent may be correlated with changes in (1) the refractive index of the medium, (2) the wavelength of absorption maxima, or (3) the rotatory strengths of particular absorption bands.

(1) *Refractive Index and Rotatory Power.*—Amongst the factors which influence rotatory power the refractive index of the medium must first be considered since the theoretical expressions[3] for rotatory power show $[\alpha]$ to depend on $(n^2 + 2)$ so that $\Omega = [\alpha]/(n^2 + 2)$ may be expected to vary less than $[\alpha]$ between solvents with different refractive indices and between different temperatures. In a number of cases[3] this is not so, and it seems that the effect of refractive index is masked by some stronger effect due to the solvent. In 3-methylhexane Ω will vary more than $[\alpha]$ between the different solvents, since $[\alpha](n - 1)$ is found to be more constant than $[\alpha]$.

Solvent	3-Methylhexane $[\alpha]^{25\cdot3}(n^{20} - 1)$ (λ 5461 Å)	3-Methylheptane [1] $[\alpha]^{18}(n^{18} - 1)$ (λ 5893 Å)
(Homogeneous)	4·3	2·7
n-Hexane	4·3	—
Benzene	4·5	2·7
CS_2	4·1	2·7
CH_2Cl_2	—	2·4 *

* Interpolated.

Calculations based on Kenyon and Platt's results[1] show that in the case of 3-methylheptane also $[\alpha](n - 1)$ is constant to within the probable experimental error. But for 9 : 10-dihydro-3 : 4-5 : 6-dibenzophenanthrene, also a hydrocarbon, there is no apparent correlation between the refractive index or the dielectric constant of the solvent and the rotatory power of the solution:

Solvent	n_D	ε^{20}	$[\alpha]^{25}$ (λ 5461 Å)
CCl_4	1·46305 (at 15°)	2·24	1265
*cyclo*Hexane	1·42900 (at 15°)	2·02	1310
Benzene	1·5033 (at 25°)	2·28	1494

Also, the rotatory power of solutions of 3-methylhexane does not depend on refractive index since $[\alpha]$ is constant for different temperatures (within the limit of accuracy).

Thus these results show that $[\alpha]$ for 3-methylhexane depends on refractive index as between different solvents but not as between different temperatures. The dependence

[1] Kenyon and Platt, *J.*, 1939, 633.
[2] Hargreaves and Richardson, *J.*, 1957, 2260.
[3] Kauzmann, Walter, and Eyring, *Chem. Reviews*, 1940, **26**, 339.

observed is not perfect and may well be fortuitous, but the fact that 3-methylheptane shows a similar dependence suggests that there may be a fundamental reason for this behaviour. In view of the wide differences in behaviour which are observed, it is noteworthy that 3-methylhexane and 3-methylheptane both obey this " rule " in the solvents studied. Against this agreement is the fact that (+)-pinane follows an opposite law, Ω being more constant than [α] as between different solvents [5] and that 9 : 10-dihydro-3 : 4-5 : 6-dibenzophenanthrene shows no dependence on refractive index.

(2) *Wavelength of Absorption Maxima and Rotatory Power.*—Changes in the wavelength of absorption maxima are, in general, far too small to account for observed changes in rotatory power. This is particularly so where the measurements are in the visible region and all the absorption bands are in the Schumann region, as in the aliphatic hydrocarbons.

(3) *Rotatory Strengths of Absorption Bands.*—Alteration in the rotatory strengths of particular absorption bands may be due to an alteration (*a*) in the proportion of the various conformational species present or (*b*) in the polarisability of the active molecule. With aliphatic hydrocarbons there is little chance that one bond will be especially affected by change of solvent, so that where the variation cannot be correlated with refractive index it seems that the observed changes in rotatory power must be due either to changes in the " average conformation " about single bonds, or to alteration in the polarisability of the molecule, but probably to the former.

In 9 : 10-dihydro-3 : 4-5 : 6-dibenzophenanthrene solutions the rotatory power cannot be correlated with the refractive index, and the solute molecule is virtually rigid, there being no possibility of change of conformation without racemisation. Yet the rotatory power varies by 20% between solutions in carbon tetrachloride and in benzene. It is noteworthy that these variations occur between solvents of zero dipole moment and low dielectric constant, and further that the concentrations used in these experiments were so small as to make solute–solute interaction virtually non-existent. A large molecule of this type is likely to be readily polarisable, so the effect of the solvent may be to alter its polarisability (the molecule also probably has a small permanent dipole moment), but the lack of dependence of [α] on refractive index is against this explanation.

It is, however, clear from this work that conformation cannot be the only influence with a major effect on the rotatory power unless the solvent can act by altering the " out-of-plane " or azimuthal angle of the solute molecule.

Effect of Temperature.—In 3-methylhexane and in octan-2-ol [6] the rotatory power of the homogeneous material varies slightly with temperature. For 3-methylhexane (homogeneous) we have:

Temp.	25·3°	40·8°	56·5°	72·3°
$[\alpha]_{5461}$	11·10°	10·96°	10·75°	10·60°
Ω_{5461} *	2·827	2·827	2·789	2·766

* Calculated by using values of n at 25·3° and $(n^2 - 1)/(n^2 + 2) = kd$.

Ω is rather more constant than [α] but with the solutions [α] varies little if at all so that Ω must be the least constant. With the 10% solutions of octanol in *n*-heptane there is still a variation with temperature but at lower concentrations this disappears. Table 1 shows that the rotatory powers of solutions of 3-methylhexane are approximately invariant with temperature. This may be attributed either (1) to the similarity of the rotatory power of the various conformations or (2) to similarity of the energy of the different conformations so that the populations of the respective forms change but little with temperature. A similar argument applies to Ω if this is considered to be the fundamental quantity, but work with the dilute solutions suggests that [α] is, in fact, the more fundamental.

Since the solvent molecules are symmetric, in dilute solutions the solute molecules are

[4] Hargreaves, *J.*, 1954, 1781.
[5] Rule and Chambers, *J.*, 1937, 145.
[6] Hargreaves, *J.*, 1953, 2953.

probably sufficiently far apart for the energy of " packing in the solution " to be much the same for all conformations so that there is invariance of rotatory power with temperature. In the homogeneous substance, however, the different conformations will have rather

TABLE 1. *Optical rotatory and refractive dispersions of* (+)-3-*methylhexane.*

Solvent	c * (g./100 c.c.)	t (°c)	Wavelength (Å) 6438	5780	5461	5086	4800	4358	$[\alpha]_{4358}$ / $[\alpha]_{5461}$
			$[\alpha]$ (l = 2, except for first set, where l = 1)						
None (homogeneous)		25·3 [a]	7·72°	9·80°	11·10°	12·95°	14·61°	18·34°	1·65
		40·8	7·53	9·73	10·96	12·74	14·43	18·05	1·65
		56·5	7·42	9·52	10·75	12·62	14·38	17·65	1·64
		72·3	7·33	9·36	10·60	12·46	14·20	17·41	1·64
n-Hexane	11·17	25·3 [b]	7·9	10·0	11·3	13·3	14·7	18·0	1·60
		39·7	7·8	9·9	11·1	13·3	14·5	17·8	1·60
		51·0	7·7	9·9	11·1	13·2	14·4	18·0	1·63
	7·58	25·3	8·0	10·0	11·1	13·2	14·8	18·1	1·63
		40·0	—	10·0	11·1	—	—	18·1	1·63
		56·4	—	10·1	11·2	—	—	18·1	1·61
Benzene	8·38	24·3	7·7	8·7	9·3	11·0	12·2	15·4	1·66
		37·7	—	8·5	9·4	—	—	15·8	1·68
		51·3	—	8·6	9·3	—	—	15·5	1·67
		65·6	—	8·7	9·2	—	—	15·4	1·65
	4·19	24·3	—	8·7	9·2	—	—	14·9	1·62
CS_2	8·30	25·3	—	6·0	6·8	—	—	10·6	1·56
		38·5	—	5·7	6·4	—	—	—	
	4·15	24·3	—	5·9	6·4	—	—	—	
		37·9	—	6·0	6·4	—	—	—	
H·CO·NHMe + $COMe_2$	7·82	24·9	—	9·6	10·4	—	—	—	
		37·8	—	9·2	10·1	—	—	—	

n (homogeneous) †

25·3	1·3853	1·3869	1·3881	1·3899	1·3917	1·3950

Densities (d_4^t)

t	25·3°	40·8°	56·5°	72·3°
d_4	0·6850	0·6716	0·6850	0·6445

* The actual values of c used were corrected for the expansion of the solution, standard values being used for the densities of the solvent except for the solution in monomethylformamide and acetone which had $d_4^{20\cdot4}$ 0·9079, $d_4^{49\cdot8}$ 0·8817. (Acetone, c = 25·89; monomethylformamide, c = 64·15.)

† n_D^{20} 1·3890, $n_{3893}^{25\cdot3}$ 1·3866.

[a] $[\alpha]_{5893}$ = 9·43° at 19·9°, 9·42° at 25·3°. [b] $[\alpha]_{5893}$ = 9·6° at 24·3°.

TABLE 2. *Specific rotatory powers* * *of* (+)-3-*methylhexane in the ultraviolet region.*

λ	$[\alpha]$	λ	$[\alpha]$	λ	$[\alpha]$	
		(a) *Homogeneous liquid* (l = 0·25)				
4326	18·57°	3305	36·09°	2754	59·45°	t = 25·3°
3856	24·41	2970	47·77	2591	71·12	
3514	30·25	2843	53·61	2529	76·96	
4294	18·92	3248	36·77	2718	60·57	t = 40·0°
3840	24·87	3100	42·72	2644	66·52	
3505	30·82	2947	48·67	2599	72·47	
4423	17·45	3180	37·44	2810	55·62	t = 54·0°
3589	28·36	3067	43·50			
		(b) *Solution in* n-*hexane* (c = 11·17; l = 1, t = 25·3°)				
3825	22·98	3490	30·65	2870	57·46	
3631	26·81	3057	45·97	2598	68·95	

* The rotatory powers are exact, the error being in the estimation of the wavelength, the line given being that nearest at match.

different energies owing to the need to pack into holes in a liquid consisting of unsymmetrical molecules. It is difficult to see in what other way a solvent of such similar character to the solute as *n*-hexane could influence the rotatory power.

Summary.—The rotatory power of solutions of 3-methylhexane depends on $(n - 1)$ in the solvents studied, but is independent of n where change of temperature is concerned. The rotatory power of the homogeneous substance varies slightly with temperature, this variation may be correlated, at least in part, with changes in refractive index. In 9 : 10-dihydro-3 : 4-5 : 6-dibenzophenanthrene, by contrast, no relation to refractive index was observed. Since only one conformation of this molecule is possible, it is difficult to explain the observed variations of rotatory power with solvent.

TABLE 3. *Rotatory dispersion of* (+)-1-*bromo*-2-*methylbutane at* 20°.

Wavelength (Å)	6438	5893	5780	5461	5086	4800	4358
$[\alpha]$ ($l = 2$)	3·32°	4·07°	4·22°	4·72°	5·44°	6·04°	7·13°

$d_4^{20\cdot0}$ 1·2232; $n_{5893}^{20\cdot0}$ 1·4450.

EXPERIMENTAL

1-*Bromo*-2-*methylbutane.*—(*a*) 2-Methylbutanol (0·46 mole), kept for 3 days at room temperature in a sealed tube with phosphorus tribromide (0·54 mole), gave the bromide, b. p. 116—122°, n_D^{20} 1·4445, in 52% yield. The product contained traces of phosphorus compounds which were difficult to remove.

(*b*) *Modification of Heller's method.*[7] (−)-2-Methylbutanol (47 g.) [$\alpha_{5461}^{20\cdot1}$ −5·748° ($l = 1$)] was saturated with dry hydrogen bromide (from boiling decalin and bromine) at 0°. The temperature was then raised to 100° and the stream of hydrogen bromide continued for 2½ hr., after which the lower layer of hydrogen bromide solution was run off. The remaining 1-bromo-2-methylbutane was washed twice with ice-water, separated, and dried by freezing. The bromide was shaken twice at 0° with an equal volume of sulphuric acid and then, also at 0°, twice with an equal volume of water. The liquid was again " freeze dried " and then left over freshly heated potassium carbonate. The product (68·2 g.) was distilled, giving the bromide (65·7 g., 81·5%), b. p. 38·3°/39 mm., $\alpha_{5461}^{20\cdot1}$ +5·483° ($l = 1$).

Fractionation. The bromide, α_{5461}^{20} +5·53° (67·6 g., from another preparation using 2-methylbutanol with α_{5461}^{20} −5·65°), was distilled from a 50 ml. flask in a water-bath at 74—79° through a 20 cm. vacuum-jacketed column, 1 cm. diam., packed with broken glass, giving (1) 11·5 g., b. p. 62—64·8°/140 mm., α +5·11° ($l = 1$), (2) 15·8 g., b. p. 65·0°/140 mm., α_{5461}^{23} +5·41° ($l = 1$), (3) 15·8 g., b. p. 65—65·6°/140 mm., α_{5461}^{20} +5·77° ($l = 1$), $[\alpha]_{5893}^{20}$ +4·068°, d_4^{20} 1·2232, n_D^{20} 1·4450 (cf. Brauns,[8] $[\alpha]_{5893}^{20}$ 4·043°, d_4^{20} 1·2234), n_D^{20} 1·4451. Dry hydrogen was passed through the " air-leak " during these preparations. The rotatory power of fraction (3) fell to α_{5461}^{20} +5·721° ($l = 1$) in 14 days, care being taken to exclude moisture.

(±)-3-*Methylhexane.*—(a) *By Heller's method.* Magnesium turnings (7·4 g.) and 1-bromo-2-methylbutane (41·7 g.) in ether (100 ml., Na-dried) under dry nitrogen were blown into an ethereal solution of diethyl sulphate (95·3 g., dried by K_2CO_3), giving a thick paste. After being refluxed and stirred for 15 hr. (shorter time reduces the yield), the cooled mixture was poured into dilute hydrochloric acid and ice. After removal of the ether from the dried ($CaCl_2$) ethereal layer, the residue was treated with an equal volume of concentrated sulphuric acid (in ice). The upper layer was kept over anhydrous potassium carbonate and distilled, giving a main fraction (10·4 g., 38%), b. p. 87·5—94°/760 mm., n_D^{15} 1·3921 (cf. below).

(b) *From ethyl-lithium.* Lithium wire (1 mm. diam., 5 g.) and dry pentane (100 ml.) under dry hydrogen were placed in a 500 ml. flask fitted with a strong stirrer and a CO_2–Methyl Cellosolve condenser (Quickfit air condenser surrounded by an inverted hot-water bottle with a sawn-off base). Ethyl chloride vapour (2 g., dried by silica gel) was added, and the solution gently warmed and stirred. When the reaction was completed a further 28·1 g. of ethyl chloride were

[7] Heller, *J. Amer. Chem. Soc.*, 1952, **74**, 4858.
[8] Brauns, *J. Res. Nat. Bur. Stand.*, 1937, **18**, 315.

added during 4 hr., the stream of dry hydrogen being maintained throughout the reaction and during subsequent refluxing for 30 min. The mixture was then filtered by blowing (with hydrogen) through a tube containing glass-wool. The filtered solution was made up to 500 ml. with dry pentane and analysed by the benzyl chloride method,[9] a yield of 77% based on lithium being indicated.

To 0·2 mole of ethyl-lithium (by titration) in 200 ml. of dry *n*-pentane under dry hydrogen, 1-bromo-2-methylbutane (15·1 g., 0·1 mole) in an equal volume of *n*-pentane was slowly added; the mixture was then slowly warmed, allowed to reflux overnight, cooled, and decomposed by pouring on crushed ice. A vigorous reaction ensued (the residue remaining in the flask was very reactive to air). The pentane layer was dried (K_2CO_3) and then fractionated through a column surrounded by warm water (*ca.* 40°), giving 3-methylhexane (1·8 g., 18%), b. p. 85—96°, n_D^{20} 1·3888 (cf. below).

(c) *From pentyl-lithium.* Lithium (5 g., as 1 mm. wire) was pressed into a 3-necked 250 ml. flask in an atmosphere of dry hydrogen, and 30 drops of a solution of 35 g. of 1-bromo-2-methylbutane [α_{5461}^{20} +5·70° (l = 1)] in 50 ml. of ether were added with stirring in the presence of a slow stream of dry hydrogen. The mixture was cooled to −10° by immersion in CO_2–acetone. The remainder of the bromide was added during 30 min., the temperature being kept at −10° to −15°. The mixture was then allowed to warm to 0° in 2 hours' standing in ice–salt. The pentyl-lithium solution was filtered through glass wool in a tube and then blown by dry hydrogen through a polyl(vinyl chloride) tube into a separating funnel, the whole apparatus being filled with dry hydrogen. The pentyl-lithium solution was run slowly into diethyl sulphate (60 g., dried by K_2CO_3) and ether (100 ml., dried by Na) in a 500 ml. 3-necked flask, cooled in ice–water when necessary to maintain moderate refluxing. The mixture was then refluxed for a further hour, cooled, and poured into dilute hydrochloric acid and ice. The ethereal layer (dried by $CaCl_2$) was fractionated from a water-bath as before. The residue was shaken with an equal volume of concentrated sulphuric acid at 0°; the upper layer was washed with a little water and dried (K_2CO_3). The crude paraffin (12·7 g.) was fractionated, giving 10·3 g., 44·4%, b. p. 86—106°/760 mm. Refractionation gave 8·3 g., b. p. 91—93°/760 mm., $[\alpha]_{5893}^{19·9}$ +9·43°, n_D^{20} 1·3892, $d_4^{19·9}$ 0·6898 (cf. Gordon and Burwell,[10] $[\alpha]_{5893}^{25}$ +9·10°, n^{20} 1·3889, d_4^{25} 0·6824; Marckwald,[11] $[\alpha]_{5893}^{20}$ +9·5°, d_4^{20} 0·6865).

Measurements.—These were carried out as previously described.[6] The observational error was probably less than 0·01° for 5461 and 5780 Å in the best cases, and about ±0·03° for the other lines. Since it is sometimes necessary to correct for different conditions, mean values for rotatory powers are given to an accuracy greater than that warranted by the individual measurements. This avoids certain losses in accuracy due to "rounding off" in the course of conversion.

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[9] Wittig, "Newer Methods of Preparative Organic Chemistry," Interscience, New York, 1948, 575.
[10] Gordon and Burwell, *J. Amer. Chem. Soc.*, 1948, **70**, 3128.
[11] Marckwald, *Ber.*, 1904, **37**, 1046.

XUM

277. *Organic Fluorine Compounds. Part X.* Reaction of Organic Compounds with Iodine in the Presence of Silver Fluoride or Trifluoroacetate.*

By Ernst D. Bergmann and Israel Shahak.

A mixture of iodine and silver fluoride causes iodine substitution of aromatic compounds and allylic positions; it can also lead to the dehydrogenation of activated aromatic compounds, such as phenol ethers and dialkylarylamines. An analogous behaviour was observed for the system silver trifluoroacetate–iodine. This system also converts primary alcohols into aldehydes and secondary alcohols into the corresponding ketones and α-dicarbonyl compounds.

The experiments reported were undertaken in the hope of obtaining fluorine-containing organic compounds by the reaction between iodine and silver fluoride in the presence of olefins and acetylenes. It had been expected that a substance such as IF might form and add to the double or triple bonds, but this was not so, although some noteworthy observations were made.

The mixture of iodine and silver fluoride, applied to an excess of the substance tested, substitutes aromatic rings and allylic positions; positive iodine is thus formed as an intermediate.[1] The *inorganic* product is a red compound of silver iodide and silver fluoride;[2] the latter must, therefore, be used in excess and the reactions can be formulated as follows:

$$(1)\ AgF + I_2 \longrightarrow AgI + I^+ + F^-;\ (2)\ I^+ + RH \longrightarrow RI + H^+;\ (3)\ AgI + AgF \longrightarrow AgI,AgF$$

Benzene gave iodobenzene in 10% yield, toluene *p*-iodotoluene in 15% yield, anisole *p*-iodoanisole in 51% yield, and 1-ethoxynaphthalene a 40% yield of the 4-iodo-derivative. From 2-methoxy- and 2-ethoxy-naphthalene, the 1-iodo-derivatives were obtained in 47 and 50% yield, respectively, accompanied by 30% of 2 : 2′-dimethoxy- and 2 : 2′-diethoxy-1 : 1′-dinaphthyl. The system silver fluoride–iodine exerts, therefore, also an oxidising action. This effect became predominant for *NN*-dialkyl aromatic amines (dimethyl-aniline, -*p*-toluidine, and -α- and -β-naphthylamine); it was observed even when silver fluoride *alone* was brought into contact with substances which produced metallic silver and compounds of the Methyl Violet type. Other silver salts which behaved analogously are the nitrate, trifluoroacetate, and (less violently) the sulphate; silver chloride, bromide, and iodide were ineffective. From dimethylaniline and silver trifluoroacetate, for example, the crystalline trifluoroacetate of Methyl Violet was obtained analytically pure; it was identified by its absorption spectrum.[3]

As to olefinic and acetylenic compounds, ethyl cinnamate, ethyl phenylpropiolate, and phenylpropiolic acid proved refractory, but ethyl crotonate, *cyclo*hexene, α-methylstyrene, propenylbenzene, 4-phenylbut-1-ene, and allylbenzene reacted smoothly. Owing to the sensitivity of the allyl-type iodides formed, only ethyl β-iodocrotonate could be isolated as such. 4-Phenylbut-1-ene gave (probably) 3-iodo-4-phenylbut-1-ene which was isolated, after reaction with benzylamine, as 3-benzylamino-4-phenylbut-1-ene hydriodide. Analogously, ethyl γ-iodocrotonate was converted into the hydriodide of ethyl γ-benzylaminocrotonate. With *cyclo*hexene, the product (3-iodo*cyclo*hexene) was identified by dehydrohalogenation to *cyclo*hexa-1 : 3-diene, isolated as its adduct with maleic anhydride.

In the same way as the system silver fluoride–iodine, iodine–silver trifluoroacetate, according to Haszeldine,[4] iodinates aromatic compounds in good yield; it has been

* Part IX, Bergmann and Cohen, *J.*, 1958, 2259.

[1] Kikindai, *Ann. Chim.* (*France*), 1956, **1**, 273.
[2] Simons, "Fluorine Chemistry," Academic Press Inc., New York, 1950, Vol. I, p. 526.
[3] Holmes, *Ind. Eng. Chem.*, 1924, **16**, 35; 1925, **17**, 918.
[4] Haszeldine, *J.*, 1952, 993; cf. Henne and Zimmer, *J. Amer. Chem. Soc.*, 1951, **73**, 1362.

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assumed that the reactive species is trifluoroacetyl hypoiodite $CF_3 \cdot CO_2I$. The analogy between the two systems is demonstrated by the fact that ethyl crotonate is converted into ethyl γ-iodocrotonate also under Haszeldine's conditions.

Haszeldine's results have been supplemented by a study of the behaviour of 1- and 2-naphthol, 1- and 2-methoxynaphthalene, and alizarin. Whilst 1-naphthol gave only an intractable product, a yield of 20% of 1-iodo-2-naphthol was obtained from 2-naphthol. The two methyl ethers differed, though only quantitatively, in their behaviour, 1-iodo-2-methoxynaphthalene being formed in 70%, 4-iodo-1-methoxynaphthalene in 15% yield. 4-Iodoalizarin was obtained in 60% yield. No oxidative effect on 2-methoxynaphthalene was observed in this case.

Primary alcohols are dehydrogenated smoothly by silver trifluoroacetate and iodine to the corresponding aldehydes; the yields were: for *n*-butanol 25%, allyl alcohol 25%, crotyl alcohol 50%, benzyl alcohol 75%, and cinnamyl alcohol 80%. The reaction with secondary alcohols is more complex. Treatment of the product formed from propan-2-ol with 2 : 4-dinitrophenylhydrazine gave a mixture of the dinitrophenylhydrazones of acetone and methylglyoxal; the latter was also obtained by the analogous reaction with acetone. Equally, from ethyl methyl ketone we obtained diacetyl (yield, 50%), from *iso*butyl methyl ketone acetyl*iso*butyryl (yield, 33%), and from acetophenone phenylglyoxal. 1-Styrylethanol gave a 40% yield of benzylideneacetone, together with polymer. These reactions are similar to those of ketones with selenium dioxide.[5] Quantitative studies have shown that the oxidation of secondary alcohols to ketones requires 2 mol. of silver trifluoroacetate and 1 mol. of iodine; the latter is recovered quantitatively as silver iodide. One can, therefore, assume the following mechanism, involving the formation of trifluoroacetyl hypoiodite:

$$CF_3 \cdot CO_2Ag + I_2 \longrightarrow CF_3 \cdot CO_2I + AgI$$
$$CF_3 \cdot CO_2I + R^1R^2CH \cdot OH \longrightarrow CF_3 \cdot CO_2H + HI + R^1R^2C{:}O$$
$$CF_3 \cdot CO_2Ag + HI \longrightarrow AgI + CF_3 \cdot CO_2H$$
$$2CF_3 \cdot CO_2Ag + I_2 + R^1R^2CH \cdot OH \longrightarrow R^1R^2C{:}O + 2CF_3 \cdot CO_2H + 2AgI$$

The transformation of ketones into 1 : 2-dicarbonyl compounds is more complicated. It often occurs only after an induction period of 5—15 min. and requires 1 mol. of iodine and 2 mol. of the silver salt. The silver iodide separates quantitatively from the organic solution, but the dicarbonyl compound can be isolated from it only after treatment with water. The overall equation is, therefore:

$$R^1 \cdot CO \cdot CH_2R^2 + 2CF_3 \cdot CO_2Ag + I_2 + H_2O \longrightarrow R^1 \cdot CO \cdot COR^2 + 2AgI + 2CF_3 \cdot CO_2H$$

Ketones form fairly stable azeotropes with trifluoroacetic acid; they boil at a higher temperature than either the ketone or the acid (b. p. 71°) and have no strictly stoicheiometric composition: the azeotrope with acetone, b. p. 108°, contains 60·2% of trifluoroacetic acid (calc., 65·0% for a 1 : 1-compound); the azeotrope with *iso*butyl methyl ketone, b. p. 132°, contains 54·0% of trifluoroacetic acid (calc., 51·9%); the azeotrope with *cyclo*hexanone, b. p. 163°, contains 44% of trifluoroacetic acid (calc., 52·4%).

When the azeotrope with *iso*butyl methyl ketone was distilled *in vacuo* (b. p. 48°/35 mm.) the distillate contained 42% of trifluoroacetic acid.

Experimental

Silver fluoride was prepared in the dark. To 25% hydrofluoric acid (80 ml.) in a Polythene beaker, silver oxide (80 g.) was added in small portions. After 30 min., the neutral mixture was filtered and evaporated in a porcelain dish. The residue was dried at 150° and kept in a desiccator. The yellowish product is very sensitive to light; it contained 0·1—0·3% of insoluble silver and 85% of total silver (calc., 85·1%). It is reduced to metallic silver by aliphatic

[5] Riley, Morley, and Friend, *J.*, 1932, 1875.

alcohols, diethyl ether, and dioxan. Reactions with silver fluoride were carried out with an excess of the substrate as solvent.

Silver trifluoroacetate was prepared by Haszeldine's method;[6] its reactions were best carried out in carbon tetrachloride or tetrachloroethylene, which are not attacked by the mixture of the salt with iodine.

Iodination of Ethyl Crotonate.—(*a*) To ethyl crotonate (40 ml.) and silver fluoride (13 g.; 0·1 mole), iodine (12·5 g.; 0·05 mole) was added in small portions and the mixture gently heated in a water-bath. After the solution had become colourless, the red precipitate was filtered off and washed with dry ether (20 ml.), and the filtrate distilled. Ethyl γ-iodocrotonate distilled at 83—85°/(1 mm. (lit.,[7] 90°/2 mm.) (yield, 2·4 g.; 20%) (Found: C, 30·9; H, 3·2. Calc. for $C_6H_9O_2I$: C, 30·0; H, 3·8%). When the filtrate was heated with benzylamine (10 g.; 0·1 mole) at 50° for some minutes, a crystalline precipitate of *ethyl α-benzylaminocrotonate hydriodide* was obtained, m. p. 175° after recrystallization from propyl alcohol (Found: C, 44·5; H, 5·7; N, 4·1. $C_{13}H_{18}O_2NI$ requires C, 44·9; H, 5·2; N, 4·0%).

(*b*) A mixture of iodine (12·5 g.; 0·05 mole) and carbon tetrachloride (50 ml.) was heated to the b. p. and quickly chilled, and silver trifluoroacetate (13 g.; 0·058 mole) and (slowly and with efficient agitation) ethyl crotonate (5·7 g.; 0·057 mole) were added. Within 10 min., the colour of the iodine disappeared; the silver iodide was filtered off and washed with carbon tetrachloride. Distillation gave ethyl γ-iodocrotonate, b. p. 83—85°/1 mm. (95 g.; 80%), identified by transformation into γ-hydroxycrotonic acid, m. p. 108°, by Glattfeld and Lee's method.[8] The amount of dry silver iodide isolated was 12·0 g. (0·05 mole); *i.e.*, half of the iodine was recovered as silver salt.

Iodination of cyclo*Hexene.*—The solution obtained from *cyclo*hexene (50 ml.), silver fluoride (13 g.), and iodine (12·5 g.) at 20—30° was diluted with light petroleum (b. p. 40—60°; 20 ml.) and refluxed with pyridine (15 ml.) for 2 hr. The product was washed with dilute hydrochloric acid, dried ($MgSO_4$), and refluxed with maleic anhydride (10 g.) for 2 hr. Upon cooling, 3 : 6-*endo*ethylene-1 : 2 : 3 : 6-tetrahydrophthalic anhydride (1·8 g.; 10%) crystallized, m. p. 147° (lit.,[9] 147°). It was identified by hydrolysis to the free dicarboxylic acid, m. p. 152° (lit.,[9] 152°).

Iodination of 4-Phenylbut-1-ene.—The product from 4-phenylbut-1-ene [10] (20 g.), silver fluoride (8·25 g.), and iodine (6·25 g.) at 20—30° was filtered and the solid phase washed with light petroleum (b. p. 40—60°; 20 ml.). To the filtrate, benzylamine (2·7 g.) was added; the precipitate of *3-benzylamino-4-phenylbut-1-ene hydrodide*, recrystallized from water, had m. p. 221° (Found: C, 55·7; H, 5·3; N, 3·8. $C_{17}H_{20}NI$ requires C, 56·0; H, 5·5; N, 3·8%). Allylbenzene,[11] propenylbenzene,[12] and α-methylstyrene [13] decolorized iodine in the presence of silver fluoride, but no definite product was isolated.

Iodination of Benzene.—The reaction between benzene (40 ml.), silver fluoride (13 g.), and iodine (12·5 g.) was carried out as above at room temperature and completed by a short heating on the water-bath. The solid was filtered off and washed with benzene (10 ml.). Distillation gave iodobenzene (2 g.; 10%), b. p. 185—186°, n_D^{20} 1·6220. In the same way, toluene gave a 15% yield of *p*-iodotoluene, b. p. 207—208°, m. p. 35°, and anisole a 57% yield of *p*-iodoanisole, b. p. 127° (20 mm.), m. p. 52°.

Iodination of 2-Methoxynaphthalene.—(*a*) At 80—90° iodine (12·5 g.) was added to a mixture of 2-methoxynaphthalene (40 g.) and silver fluoride (12 g.). After 30 min., the colour had disappeared and the liberation of hydrogen fluoride ceased. After addition of boiling benzene (150 ml.), the solid was filtered off and the liquid distilled *in vacuo*. At 95—96°/2 mm. the excess of 2-methoxynaphthalene distilled; at 141—142°/2 mm., 1-iodo-2-methoxynaphthalene [m. p. 88° after recrystallization from ethanol (lit.[14] 88°) (yield 13·5 g.; 47%) (Found: C, 46·4; H, 3·4. Calc. for $C_{11}H_9OI$: C, 46·5; H, 3·2%)]; and at 220°/2 mm., 2 : 2′-dimethoxy-1 : 1′-dinaphthyl [m. p. 190° after recrystallization from butanol (lit.[15] 190°) (yield 4·7 g.; 30%) (Found: C, 83·7; H, 6·1. Calc. for $C_{22}H_{18}O_2$: C, 84·1; H, 5·7%)].

[6] Haszeldine, *J.*, 1951, 584.
[7] Braun, *J. Amer. Chem. Soc.*, 1930, **52**, 3174.
[8] Glattfeld and Lee, *J. Amer. Chem. Soc.*, 1940, **62**, 354.
[9] Diels and Alder, *Annalen*, 1928, **460**, 98.
[10] Gilman and McGlumphy, *Rec. Trav. chim.*, 1928, **47**, 418.
[11] Hershberg, *Helv. Chim. Acta*, 1934, **17**, 351.
[12] Levy and Dvoleitzka-Gombinska, *Bull. Soc. chim. France*, 1931, **49**, 1765.
[13] Staudinger and Breusch, *Ber.*, 1929, **62**, 442.
[14] Meldola, *J.*, 1884, **45**, 156; Ray and Moomaw, *J. Amer. Chem. Soc.*, 1933, **55**, 3833.
[15] Pummerer, Prell, and Rieche, *Ber.*, 1926, **59**, 2159.

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(*b*) A mixture of iodine (12·5 g.) and carbon tetrachloride (40 ml.) was heated to the b. p. and chilled very quickly. Silver trifluoroacetate (13 g.) and 2-methoxynaphthalene (7·9 g.) were added and the mixture refluxed until the colour of the iodine had disappeared. The precipitate was filtered off and washed with ether and the filtrate washed with water, dried, and concentrated. The residue, recrystallized from ethanol, had m. p. 88° (yield, 19·9 g.; 70%).

Iodination of 2-Ethoxynaphthalene.—As for the 2-methoxy-compound, but at 40—50°, the reaction gave 2-ethoxy-1-iodonaphthalene, yield 50%, b. p. 145—146°/0·2 mm.; from ethanol, m. p. 95° (lit.,[14] 95°) (Found: C, 48·5; H, 4·0. Calc. for $C_{12}H_{11}OI$: C, 48·3; H, 3·7%), and 2 : 2′-diethoxy-1 : 1′-dinaphthyl, yield 30%, b. p. 220°/0·2 mm.; from butanol, m. p. 90° (lit.[15] 90°) (Found: C, 84·5; H, 6·8. Calc. for $C_{24}H_{22}O_2$: C, 84·2; H, 6·4%).

Iodination of 1-Ethoxynaphthalene.—The reaction was carried out as for the 2-isomer. 4-Iodo-1-ethoxynaphthalene had b. p. 180°/0·2 mm., m. p. 44° after recrystallization from ethanol (lit.,[16] m. p. 43·5°) (yield, 40%), and decomposed quickly on standing.

Iodination of 1-Methoxynaphthalene.—The reaction of 1-methoxynaphthalene with silver trifluoroacetate and iodine was carried out as described for the 2-compound. 4-Iodo-1-methoxynaphthalene had m. p. 52° (lit.,[16] 52°) after recrystallization from ethanol (yield, 15%).

Iodination of Alizarin.—Alizarin (1·2 g.), iodine (1·25 g.), and nitrobenzene (40 ml.) were heated at 120° and chilled quickly. Silver trifluoroacetate (2 g.) was added and the mass agitated for 4 hr. at room temperature and for 5 hr. at 100°. The solid was filtered off and washed with hot benzene (5 ml.). The filtrate was washed with water and after addition of light petroleum (b. p. 40—60°; 20 ml.) extracted with 15% potassium carbonate solution. The aqueous extract was acidified with hydrochloric acid and 4-iodoalizarin filtered off, after it had stood for 1 hr. at 0°, and recrystallized [m. p. 209—210° (lit.,[17] 209—210°) (yield, 1 g.; 60%)] from 90% acetic acid.

Reaction of Dimethylaniline with Silver Trifluoroacetate.—To a solution of dimethylaniline (6 g.) in methanol (15 ml.), silver trifluoroacetate (11 g.) in the same solvent (20 ml.) was added and the mixture cautiously heated until reaction set in. The black precipitate was filtered off and washed with boiling methanol (10 ml.), and the combined filtrates were concentrated to dryness. The residue was, according to the analysis and the spectrum ($\lambda_{max.}$ 550 mμ, in ethanol [3]) the *trifluoroacetate of Methyl Violet* (Found: C, 67·6; H, 6·7; N, 8·3; F, 11·9. $C_{26}H_{27}O_2F_3N_3$ requires C, 66·4; H, 6·0; N, 8·7; F, 12·1%). An analogous behaviour was observed with *NN*-dimethyl-*p*-toluidine [18] and -1- and -2-naphthylamine.[19]

Reaction of Alcohols with Silver Trifloroacetate and Iodine.—(a) n-*Butanol.* Butanol (40 g.), iodine (12·5 g.; 0·05 mole), and silver trifluoroacetate (24 g.; 0·4 mole) were stirred at room temperature until the colour of the iodine had disappeared. The silver iodide was filtered off (24 g.; 0·1 mole) and the solution fractionated. At 74—78°, 1 g. (25%) of butyraldehyde distilled (2 : 4-dinitrophenylhydrazone, m. p. 123°;[20] dimedone derivative, m. p. 134° [21]).

(b) *Allyl alcohol.* The reaction, carried out as above, gave acraldehyde, b. p. 50—54°, (yield, 25%) (2 : 4-dinitrophenylhydrazone, m. p. 165° [22]).

(c) *Crotyl alcohol.* The reaction between crotyl alcohol (36 g.), iodine (12·5 g.), and silver trifluoroacetate (24 g.) in carbon tetrachloride (50 ml.) at room temperature gave 23·5 g. of silver iodide and 1·75 g. (50%) of crotonaldehyde, b. p. 100—102° (2 : 4-dinitrophenylhydrazone, m. p. 191° [20]).

(d) *Benzyl alcohol.* From benzyl alcohol (5·5 g.), benzaldehyde (4 g.; 75%) was obtained in the same manner, b. p. 175—176° (2 : 4-dinitrophenylhydrazone, m. p. 236° [23]).

(e) *Cinnamyl alcohol.* From cinnamyl alcohol (6·6 g.), cinnamaldehyde (5·4 g.; 80%) was obtained analogously at 50—60°, b. p. 126—127/20 mm. (2 : 4-dinitrophenylhydrazone, m. p. 255° [24]).

(f) 1-*Styrylethanol.* The alcohol [25] (7·5 g.), iodine (12·5 g.), and silver trifluoroacetate

[16] Tanaka, *Chem. News*, 1925, **131**, 49; *Chem. Abs.*, 1925, **19**, 2948.
[17] Joshi, Tilak, and Venkataraman, *Proc. Indian Acad. Sci.*, 1951, **34**, 304.
[18] Hodgson and Kershaw, *J.*, 1930, 277.
[19] Gokhlé and Mason, *J.*, 1930, 1757.
[20] Huntress and Mulliken, "Identification of Pure Organic Compounds," John Wiley and Sons, New York, 1941, p. 633.
[21] Kagan, Lyubarskii, and Fedorov, *J. Appl. Chem. U.S.S.R.*, 1934, **7**, 135.
[22] Bremner, Jones, and Beaumont, *J.*, 1946, 1018.
[23] Hinkel, Ayling, and Morgan, *J.*, 1932, 2793.
[24] von Braun, Rudolph, Kroeper, and Pinkernelle, *Ber.*, 1934, **67**, 269.
[25] Meek, Lorenzi, and Cristol, *J. Amer. Chem. Soc.*, 1949, **71**, 1830.

(24 g.) in carbon tetrachloride (50 ml.) reacted at 60°; stirring was continued for 30 min. at room temperature. The filtered solution was washed with water, dried, and distilled. In addition to a dark resin, benzylideneacetone (3 g.; 40%) was obtained, b. p. 139°/25 mm. (2 : 4-dinitrophenylhydrazone, m. p. 227° [26]).

(g) *Propan-2-ol.* The reaction between propan-2-ol (40 ml.), iodine (12·5 g.), and silver trifluoroacetate (24 g.), which was added slowly at room temperature, was complete in 2 hr. The excess of the soluble silver salt was precipitated with 2 ml. of concentrated hydrochloric acid and the solution filtered and diluted with water to a total volume of 50 ml. Treatment with 2 : 4-dinitrophenylhydrazine gave a precipitate which was separated by fractional crystallization from alcohol into acetone 2 : 4-dinitrophenylhydrazone, m. p. 125°,[20] and methylglyoxal 2 : 4-dinitrophenylhydrazone, m. p. 130° [27] (Found: C, 43·6; H, 3·5; N, 22·5. Calc. for $C_9H_8O_5N_4$: C, 42·8; H, 3·2; N, 22·2%).

The structure of the second product was further proved by refluxing it (0·5 g.) with a solution of 2 : 4-dinitrophenylhydrazine (1 g.) in ethanol (100 ml.) and concentrated sulphuric acid (4 ml.), for 3 hr. Thus, the very difficultly soluble bis-2 : 4-dinitrophenylhydrazone of methylglyoxal was obtained, m. p. 300° [28] (from nitromethane) (Found: C, 41·5; H, 3·0; N, 25·7. Calc. for $C_{15}H_{12}O_8N_8$: C, 41·7; H, 2·8; N, 25·9%).

Reaction of Ketones with Silver Trifluoroacetate and Iodine.—(a) *Acetone.* To iodine (12·5 g.) suspended in carbon tetrachloride (40 ml.), silver trifluoroacetate (24 g.) and dry acetone (3 g.) were added, and the mixture was refluxed with agitation until, after about 10 min., reaction set in. When the colour had disappeared, the silver iodide (24·0 g.) was filtered off and the solution extracted three times with water (15 ml.). The combined aqueous extracts were acidified with hydrochloric acid, filtered, and heated briefly to evaporate the unchanged acetone. The methylglyoxal formed was then identified by conversion of aliquot portions of the solution into the osazone, m. p. 146°,[29] the bis-semicarbazone, m. p. 252°,[29] and the bis-2 : 4-dinitrophenylhydrazone, m. p. 300°.[28]

(b) *Ethyl methyl ketone.* The reaction was carried out, as described in the preceding paragraph, in tetrachloroethylene. Diacetyl was isolated by fractional distillation from the organic extract, b. p. 78—89° (yield, 50%); it was identified as the osazone, from nitromethane, m. p. 246° [30] (Found: C, 72·5; H, 7·0. Calc. for $C_{16}H_{18}N_4$: C, 72·2; H, 6·8%). Reaction did not occur in carbon tetrachloride.

iso*Butyl methyl ketone.* Treatment as above in carbon tetrachloride gave a 50% yield of *acetyl*iso*butyryl*, b. p. 116—118° (osazone, m. p. 115° [31]).

Acetophenone. Iodine (12·5 g.), silver trifluoroacetate, (24 g.), acetophenone (6 g.), and carbon tetrachloride (40 ml.) were heated and stirred until the colour disappeared. The filtered solution was washed with water, dried, and concentrated, and the residue dissolved in ethanol (10 ml.) and slowly poured into cold water (50 ml.). Thus, crystals of phenylglyoxal hydrate [5] were obtained, m. p. 89° [bis-semicarbazone, m. p. 220° [5] (Found: C, 48·4; H, 4·7. Calc. for $C_{10}H_{12}O_2N_6$: C, 48·4; H, 4·8%)].

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[26] Wilson and Keenan, *J. Assoc. Offic. Agric. Chemists*, 1930, **13**, 389.
[27] Fischer and Taube, *Ber.*, 1924, **57**, 1506.
[28] Neuberg and Dalmer, *Biochem. Z.*, 1925, **162**, 488.
[29] Meisenheimer, *Ber.*, 1932, **45**, 2635.
[30] von Pechmann, *Ber.*, 1888, **21**, 2754.
[31] Pauly and Lieck, *Ber.* 1900, **33**, 503.

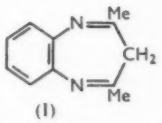
XUM

278. *The Reduction of 2-Acetyl-3-methylquinoxaline and 2 : 4-Dimethyl-1 : 5-benzodiazepine.*

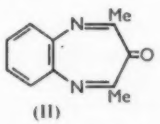
By J. A. Barltrop, C. G. Richards, and (in part) D. M. Russell.

Catalytic reduction of 2-acylquinoxalines gives deeply coloured products, which are shown to be 1 : 4-dihydro-derivatives (X) ◀▶ (XIII). The oxidation, dismutation, and further reduction of the compound (XIII; R = Me) are described. The application of nuclear magnetic resonance spectra to the determination of the structures of this compound and of the *cis*- (XIX) and the *trans*-form (XX) of 1 : 2 : 4 : 5-tetrahydro-2 : 4-dimethyl-1 : 5-benzodiazepine is illustrated.

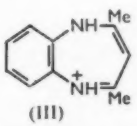
Barltrop, Richards, Russell, and Ryback have shown [1] that oxidation of 2 : 4-dimethyl-1 : 5-benzodiazepine (I) with per-acids leads to 2-acetyl-3-methylquinoxaline (IV; R = Me). During the early stages of this investigation, when it was thought that the product was the required benzodiazatropone (II), the ketone was hydrogenated in order to obtain the 3-hydroxy-1 : 5-benzodiazepine (V; R = Me).



(I)



(II)



(III)

Uptake of hydrogen was rapid over palladised charcoal and slower over Raney nickel, giving a deep crimson solution, which, under acidic conditions, assumed an intense violet colour. Reduction with tin or zinc and acid produced the same violet solution. The solutions were unstable in air, rapidly reoxidising to 2-acetyl-3-methylquinoxaline (IV; R = Me).

Stafford and Barker [2] also studied the reduction of the ketone (IV; R = Me) and reported that hydrogenation proceeds with the uptake of one *g.-atom* of hydrogen per mole giving an intensely red solution. From this and related observations they ascribe a free-radical structure to the red reduction product.

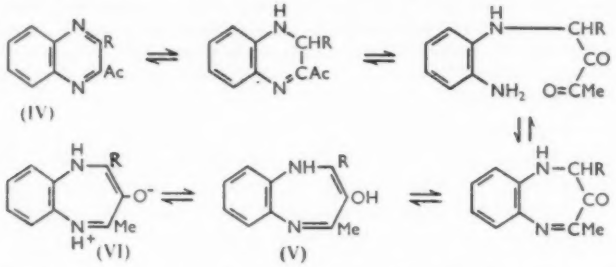
Our results differ from those of Stafford *et al.* First, with palladised charcoal and with Raney nickel, hydrogenation proceeded with no detectable break until one *mol.* of hydrogen had been absorbed. Secondly, the red solution, examined as a 0·53M-solution, was found to be diamagnetic, thus excluding the possibility that it contained any significant concentration of radical. Even when hydrogenation was stopped after the uptake of one *atom* of hydrogen, the solution was again diamagnetic. Thirdly, the dye has been isolated as red-brown needles with the analysis $C_{11}H_{12}ON_2$ expected for a dihydro-derivative. The possibility that these red needles were a dismutation product of the red component of the hydrogenated solution was eliminated by the observation that the visible spectrum of the latter was identical with that of a solution prepared from this red solid. Similar results were obtained with 2-acetyl-3-phenylquinoxaline (IV; R = Ph), from the reduction of which a purple-red dye was isolated. The infrared spectra of the solid reduction product of the methyl derivative (IV; R = Me) in Nujol showed NH or OH peaks at 3320 and 3220 cm.$^{-1}$ (as fine structure superimposed on a broad band of the type commonly ascribed to associated NH or OH groups) and C–O stretching at 958 cm.$^{-1}$, but no carbonyl group. The solid dyes were stable in air for several days.

It is clear from these results that the coloured reduction products are dihydro-derivatives of the 2-acetylquinoxalines. The dihydro-derivative (IX), which was prepared by borohydride reduction of the ketone (IV; R = Me) and was also obtained by Stafford,

[1] Barltrop, Richards, Russell, and Ryback, *J.*, 1132.
[2] Stafford and Barker, *Chem. and Ind.* 1956, 1426.

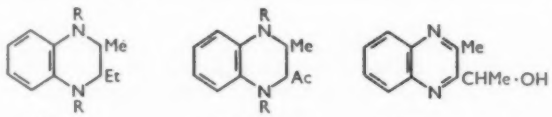
Reid, and Barker [3] by a Pondorff reduction, is a colourless solid and can be transformed into a red dye neither by acid-treatment nor by further reduction. It is likely, therefore, that reduction must occur in the heterocyclic ring if colour is to be developed.

Since the instability of the reduction products to hot dilute acid and their visible spectra were reminiscent of benzodiazepinium salts,[1] we originally proposed [4] that the reduction products were betaines (VI) derived from 3-hydroxy-1 : 5-benzodiazepines (V), possibly formed by the sequence of reversible reactions shown in the annexed formulæ.



(IV) (VI) (V)

This hypothesis now appears to be incorrect for the following reasons.* First, 2 : 4-dimethyl-1 : 5-benzodiazepine (I) is a relatively weak base,[5] so that the proton-transfer involved in the conversion of the colourless hydroxybenzodiazepine (V) into the coloured betaine is improbable. Secondly, benzodiazepinium cations appear [1,6] to be in hydrolytic equilibrium with *o*-phenylenediamine and the corresponding β-diketones, reacting with phenylhydrazine to give the appropriate phenylpyrazoles. The reduction product derived from the ketone (IV; R = Me), however, undergoes a redox reaction with phenylhydrazine giving aniline and the phenylhydrazone of the initial ketone. Thirdly, although 2 : 4-



(VII) (VIII) (IX)

dialkyl-1 : 5-benzodiazepines undergo ring-contraction to 2-alkylbenziminazoles when warmed in acid solution, the reduction product derived from the ketone (IV; R = Me), under similar conditions, gives no 2-methylbenziminazole but only small amounts of the *cis*- and the *trans*-form of 2-ethyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline, isolated as their dibenzoyl derivatives (VII; R = Bz). Further, the postulated ring-expansion to the seven-membered betaine requires the participation of water. This substance is not involved since the ketone (IV; R = Me) in dry light petroleum over palladised charcoal rapidly absorbed one mol. of hydrogen, giving a colourless solution with the red reduction product adsorbed on the catalyst from which it could be eluted with dry ethanol or dry dioxan.

That the red dye is a dihydroquinoxaline became probable when it was found that in boiling ethanol, under nitrogen, in the presence but not the absence of palladised charcoal, it underwent dismutation to a mixture of 2-acetyl-3-methylquinoxaline, 2-acetyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline (VIII; R = H), and 2-1′-hydroxyethyl-3-methylquinoxaline (IX). Chromatography showed the absence of these products from the

* We are indebted to a Referee for helpful comment on some of these points.

[3] Stafford, Reid, and Barker, *Chem. and Ind.*, 1956, 765.
[4] Barltrop and Richards, *ibid.*, 1957, 1011.
[5] Schwarzenbach and Lutz, *Helv. Chim. Acta*, 1940, **23**, 1159.
[6] Thiele and Steimmig, *Ber.*, 1907, **40**, 955.

ethanol solution before the heating. Proof of the six-membered ring structure for the coloured reduction product of the ketone (IV; R = Me) was obtained from a study of the nuclear magnetic resonance spectrum of the dyestuff (all such spectra were measured at 29·92 Mc.p.s, the accuracy of the measurements being 5% or better). Unlike a dihydroquinoxaline, the diazepinium betaine formulation (VI) has a symmetrical distribution of methyl groups and would therefore be expected to have one methyl proton resonance absorption only. 2 : 4-Dimethyl-1 : 5-benzodiazepine (I) and the ketone (IV; R = Me) were taken as models for the alternative structures. The spectrum of the former (I) (Fig. 1) showed a single intense band due to the six identical protons of its methyl groups 1·1

FIG. 1.

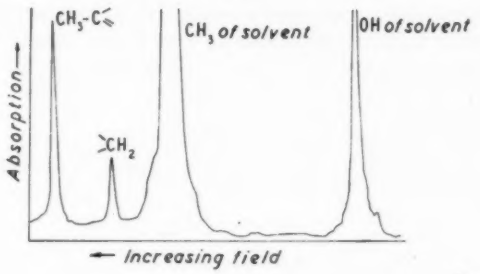
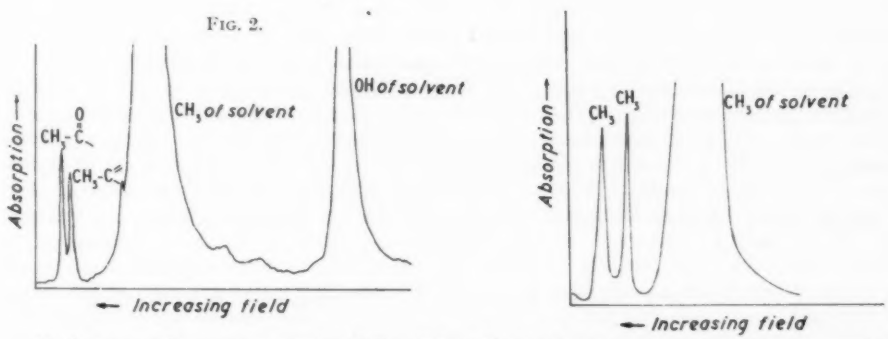


FIG. 3.

FIG. 2.

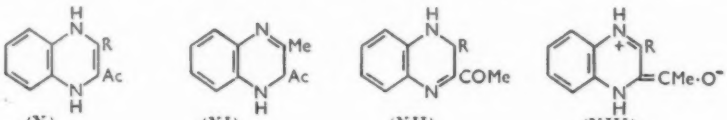


Nuclear magnetic resonance spectra of (FIG. 1) *2 : 4-dimethyl-1 : 5-benzodiazepine,* (FIG. 2) *2-acetyl-3-methylquinoxaline, both in methanol, and* (FIG. 3) *2-acetyl-1 : 4-dihydro-3-methylquinoxaline, in dimethylformamide.*

parts per million (p.p.m.) from the methyl absorption of the solvent methanol. The spectrum (Fig. 2) of the ketone (IV; R = Me) had two bands 0·07 p.p.m. apart, the one at lower field strength being 0·6 p.p.m. from the methyl absorption of the solvent, the methyl groups having different environments in this molecule. The reduction product in dimethylformamide had two methyl absorption bands 0·3 p.p.m. apart, the one at lower field strength being 0·7 p.p.m. from the solvent methyl band (Fig. 3) which is itself displaced 0·6 p.p.m. towards higher fields from the methyl band of methanol. The reduction product is therefore a dihydroquinoxaline. Of the three structures possible for such a system the isomer (XII; R = Me) can be eliminated on the grounds that it should give rise to three methyl bands: a singlet due to the $CH_3{\cdot}CO$ grouping and a doublet due to the splitting of the methyl band of the group $CH_3{\cdot}CH<$ by the adjacent single proton. The relative intensities of these bands would be 2 : 1 : 1. Structures (X; R = Me) and (XI) are both consistent with the number and relative intensities of the methyl absorption

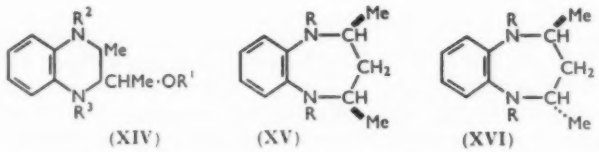
bands found in the nuclear magnetic resonance spectrum of the reduction product, but the latter structure affords no adequate explanation of the colour. We must therefore conclude that, in dimethylformamide, the reduction product exists mainly, or even exclusively, in the form (X; R = Me), the colour presumably arising from resonance with the polar canonical form (XIII). However, on present evidence, one cannot exclude the possibility that the tautomeric forms (XI) and (XII; R = Me) may contribute significantly in other solvents or under other conditions. The coloured reduction product derived from 2-acetyl-3-phenylquinoxaline is, by analogy, assigned the structure (X ⟷ XIII; R = Ph).

The relative positions of the absorption bands due to the methyl groups in the above nuclear magnetic resonance spectra are explicable on the basis that an increase of electron density in the vicinity of such a group causes shielding which is manifested by a displacement of the band in the direction of increasing field strength. Thus, the greater separation of the two methyl bands in the reduction product (X ⟷ XIII; R = Me) by comparison



with the initial ketone (IV; R = Me) is attributable to the greater negative charge on the carbonyl-oxygen atom in the former, which leads to a shift to higher fields. Also the electrophilic character of aromatic rings, which is the reason why the methyl band of toluene is at lower field strength [7] than the corresponding band for methyl*cyclo*hexane, is presumably the factor causing both methyl bands of the acetylquinoxaline (IV; R = Me) to be at lower field strengths than the corresponding bands for the reduction product.

The complete reduction of the ketone (IV; R = Me) was investigated in order to provide chemical confirmation of the dihydroquinoxaline structure for the red reduction product. Over Raney nickel or palladised charcoal, hydrogenation proceeded slowly until the disappearance of the red colour, with the uptake of between three and four mols. of hydrogen. The products could only satisfactorily be identified by benzoylation of the oil thus obtained under Schotten–Baumann conditions followed by chromatography. This yielded an *ON*-dibenzoyl derivative of 1 : 2 : 3 : 4-tetrahydro-2-1′-hydroxyethyl-3-methylquinoxaline (XIV; $R^1 = R^2 = Bz$, $R^3 = H$; or $R^1 = R^3 = Bz$, $R^2 = H$) and 1 : 4-dibenzoyl-2-ethyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline (VII; R = Bz). The structure of the latter compound follows from the fact that it is identical with neither the *cis*- nor the *trans*-form of the dibenzoyltetrahydrobenzodiazepine (XV and XVI; R = Bz) which are described below.



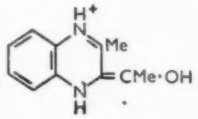
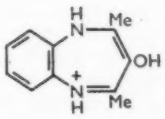
A repetition of this reduction, followed by benzoylation in pyridine, gave a dibenzoyl derivative (VII; R = Bz), the tribenzoyl derivative (XIV; $R^1 = R^2 = R^3 = Bz$), m. p. 205—206°, 2-acetyl-1 : 4-dibenzoyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline (VIII; R = Bz), and a monobenzoyl derivative, which is provisionally assigned the structure (XIV; $R^1 = R^3 = H$, $R^2 = Bz$) since the OH and NH stretching bands in its infrared spectrum were sharp and showed no evidence of hydrogen-bonding. The last compound

[7] Meyer, Saika, and Gutowsky, *J. Amer. Chem. Soc.*, 1953, **75**, 4567.

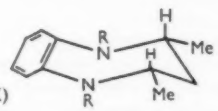
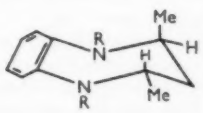
on benzoylation gave another isomer, m. p. 175°, of the tribenzoyl derivative (XIV; $R^1 = R^2 = R^3 = Bz$).

This accumulation of evidence leaves no serious doubt that the red reduction product derived from acetylmethylquinoxaline is anything other than the dihydroquinoxaline (X ⟷ XIII; R = Me). However, with acid, it changes to a purple compound, whose visible spectrum in form, in position, and in intensity ($\lambda_{max.}$ 5400 Å, ε 2300) corresponds approximately to that of dimethylbenzodiazepinium salts (III) ($\lambda_{max.}$ 5100, ε 830) (because of the extremely rapid oxidation of dilute solutions of the reduction product, it was not possible to record its spectrum in the ultraviolet region). This raises the question whether this purple substance has a dihydroquinoxaline structure (XVII) or the alternative 3-hydroxybenzodiazepinium cation structure (XVIII) formed by the reaction sequence (X) ⟶ (V) ⟶ (VI) ⟶ (XVIII) postulated earlier. However, hydrogenation of the ketone (IV; R = Me) under acidic conditions until the purple colour had been discharged led to the same products as had been formed under neutral conditions, (XIV; $R^1 = R^2 = R^3 = H$) and tetrahydroethylmethylquinoxaline (VII; R = H) being isolated as their monobenzoyl derivatives, thus disposing of the seven-membered ring structure.

For comparison, the *cis*- (XV; R = H) and the *trans*-form (XVI; R = H) of tetrahydrodimethylbenzodiazepine were required. They were obtained by hydrogenation of the dimethylbenzodiazepine followed by chromatography and were characterised as their benzoyl derivatives.

(XVII)   (XVIII)

The configurations of these isomers were assigned by examination of the nuclear magnetic resonance spectra of the two dibenzoyl derivatives (XV and XVI; R = Bz) in ethanol-free chloroform. The high molecular weight of these compounds limited the absorptions recorded to the methyl bands, which occurred in the region expected for a methyl group attached to a saturated carbon atom. The higher-melting derivative showed two peaks of equal intensity 6·3 c./sec. apart, and the other, three peaks with a separation of 6·5 c./sec., the centre one being of greatest intensity. Since a methyl band would be split into a doublet

(XIX)   (XX)

by spin–spin interaction with the adjacent CH group, the triplet must arise from the superimposition of two distinct doublets, one band of each being approximately coincident. The triplet splitting of the methyl band by the CH_2 group would be a second-order effect only, the expected magnitude of which would be less than 1 c./sec. This was not resolved and was responsible only for the broadening of each line. In the *cis*-form (XIX) the methyl groups have identical (presumably pseudoequatorial) conformations, but in the *trans*-form (XX) one group is pseudoaxial and thus has a different environment from the other. The *trans*-isomer will therefore produce a triplet absorption, and this configuration may be assigned to the lower-melting derivative and parent compound.

Experimental

Unless otherwise specified, alumina refers to Spence's grade H alumina deactivated with 5% of 10% aqueous acetic acid.

2-*Acetyl*-1 : 4-*dihydro*-3-*methylquinoxaline*.—2-Acetyl-3-methylquinoxaline (0·5 g.) in dry ethanol (50 c.c.) was hydrogentated over 5% palladised charcoal (which had been pre-equilibrated with hydrogen) until one mol. of hydrogen had been absorbed, then filtered from catalyst under nitrogen and evaporated under reduced pressure of nitrogen on a water-bath at 40°. The solid residue was washed with ether under nitrogen and dried *in vacuo*. The *dihydroquinoxaline* formed red-brown needles, m. p. 149—151° (*in vacuo*) (Found: C, 70·1; H, 6·5; N, 14·7. $C_{11}H_{12}ON_2$ requires C, 70·2; H, 6·4; N, 14·9%), $\lambda_{max.}$ 4895 Å in EtOH. The crystals were oxidised in two days in the air to 2-acetyl-3-methylquinoxaline, identified by m. p. and mixed m. p. 86—87° and by its infrared spectrum. Solutions of the reduction product are oxidised very rapidly to the same compound, but acidified solutions are stable for a few hours.

Absorption spectrum (with D.M.R.). 2-Acetyl-3-methylquinoxaline (50 mg.) was dissolved in methanol (400 c.c.) and 48% hydrobromic acid (0·5 c.c.). Hydrogen was bubbled through 4 c.c. portions of this solution contained in a test-tube with a little platinum oxide catalyst. When the developing purple colour was judged visually to have attained its maximum intensity, the solution was decanted from catalyst and the optical density at a preset wavelength was measured on a Unicam spectrophotometer. This sequence of operations was repeated several times at each wavelength, the maximum value being accepted as the optical density at that wavelength. The results, when plotted, fell on a smooth curve with $\lambda_{max.}$ 5400 Å (ε 2300).

2-*Acetyl*-1 : 4-*dihydro*-3-*phenylquinoxaline*.—2-Acetyl-3-phenylquinoxaline [1] (0·5 g.) in ethanol (50 c.c.) was hydrogenated over 5% palladised charcoal (100 mg.) until one mol. of hydrogen had been absorbed, then worked up as above. The *product* was obtained as purple-red needles, m. p. 181—182° (*in vacuo*) (Found: C, 76·8; H, 5·6; N, 11·1. $C_{16}H_{14}ON_2$ requires C, 76·8; H, 5·6; N, 11·2%), ν (in Nujol) 3350, 3250 cm.$^{-1}$, $\lambda_{max.}$ 5130 Å in EtOH. The solution in ethanol was oxidised very rapidly to the starting ketone, identified by m. p., mixed m. p. 111—112°, and infrared spectrum.

Further Reduction of 2-*Acetyl*-3-*methylquinoxaline*.—(*a*) 2-Acetyl-3-methylquinoxaline (500 mg.) in ethanol (50 c.c.) with 5% palladised charcoal (200 mg.) absorbed 232 c.c. of hydrogen (3·54 mols.) during 30 hr., the solution becoming colourless. The product, an oil (440 mg.), was shaken with benzoyl chloride and 2N-sodium hydroxide, isolated with ether, and chromatographed on alumina (140 g.) in 1 : 1 benzene–light petroleum. Prisms (15 mg.), m. p. 238—240°, from benzene–light petroleum were obtained, followed by 1- or 4-*benzoyl*-2-1′-*benzoyloxyethyl*-1 : 2 : 3 : 4-*tetrahydro*-3-*methylquinoxaline* as an oil which was obtained crystalline (50 mg.; m. p. 200—202°) from benzene–light petroleum (Found: C, 75·9; H, 6·1; N, 7·5%; *M*, 405. $C_{25}H_{24}O_2N_2$ requires C, 75·0; H, 6·0; N, 7·0%; *M*, 400), ν (in Nujol) 3340, 1720, 1638 cm.$^{-1}$. Continued elution with the same solvent gave 1 : 4-*dibenzoyl*-2-*ethyl*-1 : 2 : 3 : 4-*tetrahydro*-3-*methylquinoxaline*, *isomer A* (110 mg.), m. p. 178—179° (from benzene–light petroleum) (Found: C, 77·9; H, 6·5; N, 6·9. $C_{25}H_{24}O_2N_2$ requires C, 78·1; H, 6·3; N, 7·3%), ν (in Nujol) 1645 cm.$^{-1}$.

(*b*) 2-Acetyl-3-methylquinoxaline (800 mg.) was hydrogenated as in the immediately preceding experiment and benzoylated by boiling it for 40 min. under reflux with benzoyl chloride (0·8 c.c.) and pyridine. Isolation with ether gave an oil, which when washed with benzene (25 c.c.) gave yellow 1-*benzoyl*-1 : 2 : 3 : 4-*tetrahydro*-3-1′-*hydroxyethyl*-2-*methylquinoxaline* (480 mg.), m. p. 188—189° (from aqueous methanol) (Found: C, 72·9; H, 6·6; N, 9·9. $C_{18}H_{20}O_2N_2$ requires C, 73·0; H, 6·8; N, 9·5%), ν (in Nujol) 3440, 3390, 1613 cm.$^{-1}$. The compound is dimorphic, being reversibly converted by crystallisation from benzene into a colourless form, m. p. 196—198°, ν (in Nujol) 3450, 3330, 1600 cm.$^{-1}$. Both forms have the same ultraviolet and infrared absorptions, ν (in $CHCl_3$) 3600, 3440, 1633 cm.$^{-1}$. This monobenzoyl derivative (80 mg.) was boiled for 45 min. in pyridine with benzoyl chloride (1·5 c.c.); the product was isolated with ether and chromatographed on alumina (20 g.) with 1 : 1 benzene–light petroleum, yielding 1 : 4-*dibenzoyl*-2-1′-*benzoyloxyethyl*-1 : 2 : 3 : 4-*tetrahydro*-3-*methylquinoxaline* (*isomer A*) as an oil which separated from benzene–light petroleum in crystals (60 mg.), m. p. 175° (Found: C, 75·9; H, 5·5; N, 5·4. $C_{32}H_{28}O_4N_2$ requires C, 76·2; H, 5·6; N, 5·6%), ν (in Nujol) 1730 and 1657 cm.$^{-1}$.

The benzene-soluble material was chromatographed on alumina (80 g.). Elution with 1 : 1 benzene–light petroleum gave an orange oil A (110 mg.); further elution with benzene gave an oil B (140 mg.), and 1 : 5 ether–benzene gave an oil C (330 mg.). Washing the column finally with ether gave more 1-benzoyl-1 : 2 : 3 : 4-tetrahydro-3-1′-hydroxyethyl-2-methylquinoxaline (90 mg.), m. p. 188—189°. The oil A was boiled under reflux for 1 hr. with pyridine and benzoyl

XUM

chloride (0·5 c.c.); isolation with ether and chromatography on alumina (15 g.) in 1 : 1 benzene–light petroleum gave *2-acetyl-1 : 4-dibenzoyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline* (70 mg.), m. p. 116° (from benzene–light petroleum) (Found: C, 74·4; H, 5·6; N, 6·2. $C_{25}H_{22}O_3N_2$ requires C, 75·4; H, 5·6; N, 7·0%), ν (in Nujol) 1690 and 1648 cm.$^{-1}$. Continued development gave 1 : 4-dibenzoyl-2-ethyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline (50 mg.), m. p. 178—179° (from benzene–light petroleum). Similar treatment of oil B gave more of this dibenzoyltetrahydroquinoxaline (40 mg.). Oil C, when benzoylated in boiling pyridine with benzoyl chloride (1 c.c.), gave an oil which on crystallisation from benzene–light petroleum gave 1 : 4-*dibenzoyl-2-1′-benzoyloxyethyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline* (*isomer B*) (290 mg.), m. p. 205—206°, depressed on admixture with isomer A to 160—163° (Found: C, 76·6; H, 5·7; N, 5·3%), ν (in Nujol) 1710, 1660, and 1645 cm.$^{-1}$.

(*c*) 2-Acetyl-3-methylquinoxaline (500 mg.) in ethanol (40 c.c.) and concentrated hydrochloric acid (0·25 c.c.) with 5% palladised charcoal (200 mg.) absorbed hydrogen (227 c.c., 3·60 mols.) during 3 hr. with the discharge of the initial intense purple colour. Benzoylation in boiling pyridine with benzoyl chloride (2 c.c.) followed by chromatography on alumina (150 g.) with 1 : 1 benzene–light petroleum gave 1- or *4-benzoyl-2-ethyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline* (210 mg.), m. p. 156—157° (from benzene–light petroleum) (Found: C, 77·1; H, 7·2; N, 9·7. $C_{18}H_{20}ON_2$ requires C, 77·1; H, 7·2; N, 10·0%), ν (in Nujol) 3330 and 1618 cm.$^{-1}$. This compound (200 mg.), heated under reflux for 1 hr. with benzoyl chloride (0·5 c.c.) in pyridine, gave 1 : 4-dibenzoyl-2-ethyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline (170 mg.) which separated from benzene–light petroleum with m. p. 178—179°, alone and when mixed with a specimen of the same compound obtained from experiment (*a*) above.

Further elution with ether yielded the above 1-benzoyl-1 : 2 : 3 : 4-tetrahydro-3-1′-hydroxyethyl-2-methylquinoxaline (160 mg.), m. p. 188—189°.

2-1′-Hydroxyethyl-3-methylquinoxaline.—2-Acetyl-3-methylquinoxaline (0·5 g.) in methanol (25 c.c.) was shaken for 30 min., then boiled under reflux for 30 min., with a solution of potassium borohydride (0·4 g.) in methanol (50 c.c.) and water (25 c.c.). The mixture was acidified with acetic acid (30 c.c.) and water (200 c.c.), then basified. The product, isolated with ether, was chromatographed on alumina (30 g.) in 1 : 1 benzene–light petroleum, giving starting material (70 mg.) followed by *2-1′-hydroxyethyl-3-methylquinoxaline* (270 mg.), m. p. 81° (from ligroin) (Found: C, 69·9; H, 6·3; N, 14·7. $C_{11}H_{12}ON_2$ requires C, 70·2; H, 6·4; N, 14·9%), ν (in Nujol) 3230 cm.$^{-1}$. Benzoylation in pyridine gave *2-1′-benzoyloxyethyl-3-methylquinoxaline*, needles, m. p. 144° (from methanol) (Found: N, 9·9. $C_{18}H_{16}O_2N_2$ requires N, 9·6%).

Reaction of 2-Acetyl-1 : 4-dihydro-3-methylquinoxaline with Phenylhydrazine.—The hydrogenation of 2-acetyl-3-methylquinoxaline (500 mg.) in ethanol (50 c.c.) over palladised charcoal was stopped after the absorption of 1 mol. of hydrogen. Phenylhydrazine (0·54 c.c., 2 mol.) and concentrated hydrochloric acid (0·3 c.c.) were added and the whole was shaken in an atmosphere of nitrogen until the red colour was discharged (3 hr.), then made alkaline and steam-distilled. The distillate gave an oil, which was warmed with cupric sulphate solution to destroy any phenylhydrazine, then treated with aqueous ammonia. Aniline was isolated with ether and identified by conversion into phenylazo-β-naphthol (300 mg.), m. p. and mixed m. p. 133°.

The involatile residue from the steam-distillation was isolated with ether and crystallised from aqueous methanol, giving 2-acetyl-3-methylquinoxaline phenylhydrazone (480 mg.), m. p. 175—176°. Similar results were obtained from a solution which had been filtered from catalyst before treatment with phenylhydrazine.

Decomposition of 2-Acetyl-1 : 4-dihydro-3-methylquinoxaline by Acid.—A solution of 2-acetyl-3-methylquinoxaline (500 mg.) in ethanol (50 c.c.) was hydrogenated over palladised charcoal until one mol. had been absorbed. Then, in the presence of the catalyst, it was treated with deoxygenated water (20 c.c.) and concentrated hydrochloric acid (0·5 c.c.) and boiled under nitrogen until the purple colour disappeared (*ca.* 10 min.). Chromatography of the product on alumina (60 g.) with light petroleum gave two orange oils, A (330 mg.) and B (160 mg.). Benzoylation of oil A in pyridine followed by chromatography on alumina (20 g.) gave 1 : 4-dibenzoyl-2-ethyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline, isomer A (15 mg.), m. p. 178—179°, as the only identifiable product. Similar treatment of oil B gave 1 : 4-*dibenzoyl-2-ethyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline, isomer B*, as an oil (100 mg.) which formed crystals (25 mg.), m. p. 183—184° (from benzene–petroleum), mixed m. p. with isomer A, 154—156° (Found: C, 77·9; H, 5·9. $C_{25}H_{24}O_2N_2$ requires C, 78·1; H, 6·3%). A similar decomposition, conducted in the absence of catalyst, gave no identifiable products.

Dismutation of 2-Acetyl-1 : 4-dihydro-3-methylquinoxaline.—The hydrogenation of 2-acetyl-3-methylquinoxaline (1 g.) in ethanol (50 c.c.) over palladised charcoal was stopped after the absorption of one mol., and 20 c.c. of the reduced solution were allowed to reoxidise in air. Chromatography then yielded only starting material. The remainder of the reduced solution was heated under nitrogen, together with the catalyst, until decolorised (3½ hr.), and the product was chromatographed on alumina (18 g.) with light petroleum, 2-acetyl-3-methylquinoxaline (460 mg.) and an oil A (250 mg.) being obtained. Further elution with 1 : 1 benzene–light petroleum gave an oil B (100 mg.).

Chromatography on alumina (50 g.) in 1 : 1 benzene–light petroleum of the product obtained by benzoylating oil A gave 2-1′-benzoyloxy-3-methylquinoxaline (170 mg.), m. p. and mixed m. p. 144° (from methanol), and 2-acetyl-1 : 4-dibenzoyl-1 : 2 : 3 : 4-tetrahydro-3-methylquinoxaline as an oil (100 mg.), which formed crystals (40 mg.), m. p. 116°, from benzene–light petroleum. Similar treatment of oil B gave more 2-1′-benzoyloxy-3-methylquinoxaline (105 mg.).

The reduced solution, when heated under nitrogen in the absence of catalyst, was decolorised only very slowly and acetylmethylquinoxaline was the only product isolated.

Reduction of 2 : 4-Dimethyl-1 : 5-benzodiazepine.—(*a*) 2 : 4-Dimethyl-1 : 5-benzodiazepine (1·0 g.) in ethanol (50 c.c.) with 5% palladised charcoal (100 mg.) absorbed hydrogen (283 c.c., 1·03 mol.) during 30 hr. The oily product was benzoylated in 2N-sodium hydroxide and chromatographed on alumina (100 g.) in 2 : 1 benzene–light petroleum, giving 1-*benzoyl*-1 : 2 : 4 : 5-*tetrahydro*-cis-2 : 4-*dimethyl*-1 : 5-*benzodiazepine* (590 mg.), m. p. 156° (from benzene–light petroleum) (Found: C, 77·3; H, 7·2; N, 9·8. $C_{18}H_{20}ON_2$ requires C, 77·1; H, 7·2; N, 10·0%), ν (in Nujol) 3360, 1630 cm.$^{-1}$. Benzoylation of this compound (350 mg.) in pyridine followed by chromatography over alumina (25 g.) in 1 : 1 benzene–light petroleum gave 1 : 5-*dibenzoyl*-1 : 2 : 4 : 5-*tetrahydro*-cis-2 : 4-*dimethyl*-1 : 5-*benzodiazepine* (250 mg.), m. p. 161—162° (from benzene–light petroleum) (Found: C, 78·6; H, 6·3; N, 7·2. $C_{25}H_{24}O_2N_2$ requires C, 78·1; H, 6·3; N, 7·3%), ν (in Nujol) 1640 cm.$^{-1}$.

(*b*) The above hydrogenation was repeated on the dimethylbenzodiazepine (2·5 g.), but the product, without benzoylation, was immediately chromatographed on alumina (150 g.) in light petroleum, giving 1 : 2 : 4 : 5-*tetrahydro*-trans-2 : 4-*dimethyl*-1 : 5-*benzodiazepine*, an oil (350 mg.), b. p. 72—74°/0·075 mm. (Found: C, 74·5; H, 8·9; N, 16·4. $C_{11}H_{16}N_2$ requires C, 75·0; H, 9·1; N, 15·9%), ν (in Nujol) 3330 cm.$^{-1}$. Benzoylation in pyridine gave an oil, which was chromatographed in 1 : 1 benzene–light petroleum on alumina (70 g.), to give 1 : 5-*dibenzoyl*-1 : 2 : 4 : 5-*tetrahydro*-trans-2 : 4-*dimethyl*-1 : 5-*benzodiazepine*, m. p. 129—130° (from benzene–light petroleum) (Found: C, 78·4; H, 6·6; N, 6·9. $C_{25}H_{24}O_2N_2$ requires C, 78·1; H, 6·3; N, 7·3%), ν (in Nujol) 1640 cm.$^{-1}$.

Continued elution of the column with 1 : 5 benzene–light petroleum gave 1 : 2 : 4 : 5-*tetrahydro*-cis-2 : 4-*dimethyl*-1 : 5-*benzodiazepine* (1·64 g.), m. p. 57° (from ligroin) (Found: C, 74·3; H, 9·2; N, 16·0. $C_{11}H_{16}N_2$ requires C, 75·0; H, 9·1; N, 15·9%), ν (in Nujol) 3350 cm.$^{-1}$. Benzoylation in pyridine gave an oil which was chromatographed on alumina. Elution with 1 : 1 benzene–light petroleum gave the monobenzoyl derivative, m. p. 156°. Further elution with benzene gave the dibenzoyl derivative, m. p. 161—162°.

We are indebted to Mr. J. B. Lean and to Dr. R. E. Richards for recording the nuclear magnetic resonance spectra and for valuable discussions on their interpretation, to Mr. F. R. McKim for measurements of magnetic susceptibility, and to the Ministry of Education for a Scholarship (to C. G. R.).

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279. *Interaction between Carbonyl Groups and Biologically Essential Substituents. Part I. The Effect of Ketones on Optically Active Amino-derivatives.*

By F. Bergel, G. E. Lewis, S. F. D. Orr, and (Miss) J. Butler.

Mutarotation has been shown to occur when a number of optically active α-amino-esters, and one amine, are dissolved in ketones. The magnitude and the rate of this time-consuming change depend on the ketone used. With the L- and D-enantiomorphs so far tested, this change has been respectively towards higher negative and positive values of α. *cyclo*Pentanone and L-tyrosine ethyl ester yield a crystalline azomethine; this and infrared absorption measurements on mixtures of *cyclo*hexanone and (+)-amphetamine have given some insight into the mechanism of this interaction under mild conditions.

The interaction between carbonyl groups and groups such as NH_2 and SH in biologically important compounds has been widely studied from chemical and biochemical angles, *e.g.*, interaction of aldehydes and ketones and of amino-groups in the biosynthesis of alkaloids,[1] and the interconversion of α-amino-acids and keto-acids [2] in transamination and decarboxylation in presence of pyridoxal and pyridoxamine derivatives. The latter series of reactions has been explored in model experiments by, *e.g.*, Snell,[3] Metzler, Ikawa, and Snell,[4] and Christensen.[5] The degradation of α-amino-acids by carbonyl compounds *in vitro* has been reviewed by Schönberg and Moubacher,[6] and investigated more recently by Spenser *et al.*[7] and others; the reaction between sugars and amino-acids has been examined by Lewin [8] and between hydroxy-ketones and amino-acids by Hurd and Buess.[9] Even more interesting biologically may be intramolecular transannular interaction in peptides which is under study by means of models [10] and natural products.[11]

The effects of aldehydes and ketones on the optical rotatory powers of amino-acids have formed the subjects of a number of publications most of which have been recently discussed by Hargreaves and Richardson.[12] Two teams claimed mutarotation under their experimental conditions: Gulland and Mead [13] found such an effect with D-phenylalanine sodium salt and 2 : 3-, 2 : 5-, and 3 : 4-dimethoxybenzaldehyde in 50% aqueous ethanol, and Loiseleur and Crovisier [14] with amino-acids and formaldehyde at pH 7.

In a preliminary communication [15] we reported similar results with amino-acid esters, and (+)-amphetamine (2-amino-1-phenylpropane) in presence of ketones under practically anhydrous conditions. These observations, which are presented in Tables 1 and 2, indicated that various optically active α-amino-esters, one α-amino-amide, and one

[1] Robinson, "The Structural Relations of Natural Products," 1955, Clarendon Press, Oxford; Manske, *J.*, 1954, 2987; James, in "The Alkaloids, Chemistry and Physiology," ed. Manske and Holmes, 1950, Acad. Press, New York, Vol. I, p. 56.
[2] Williams *et al.*, "The Biochemistry of B Vitamins," Amer. Chem. Soc. Monograph, No. 110, 1950, p. 652.
[3] Snell, *J. Amer. Chem. Soc.*, 1945, **67**, 194.
[4] Metzler, Ikawa, and Snell, *ibid.*, 1954, **76**, 648.
[5] Christensen, *ibid.*, 1958, **80**, 99.
[6] Schönberg and Moubacher, *Chem. Rev.*, 1952, **50**, 261.
[7] Spenser, Crawhall, and Smyth, *Chem. and Ind.*, 1956, 796.
[8] Lewin, *Biochem. J.*, 1956, **63**, 14.
[9] Hurd and Buess, *J. Amer. Chem. Soc.*, 1956, **78**, 5667.
[10] Cohen and Witkop, *ibid.*, 1955, **77**, 6595; Anet, Bailey, and Robinson, *Chem. and Ind.*, 1953, 944; Leonard *et al.*, *J. Amer. Chem. Soc.*, 1954, **76**, 630, 3463, 5708; 1958, **80**, 4858.
[11] Grob and Meier, *Helv. Chim. Acta*, 1956, **39**, 776; Stoll, Hofmann, and Petrzilka, *ibid.*, 1951, **34**, 1544; Wrinch, *Nature*, 1957, **180**, 502; Hausmann, Weisiger, and Craig, *J. Amer. Chem. Soc.*, 1955, **77**, 723.
[12] Hargreaves and Richardson, *J.*, 1957, 3823.
[13] Gulland and Mead, *J.*, 1935, 210.
[14] Loiseleur and Crovisier, *Bull. Soc. Chim. biol.*, 1942, **24**, 241.
[15] Bergel and Lewis, *Chem. and Ind.*, 1955, 774.

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optically active amine, when dissolved in ketones, interacted there, with the rotatory power of the solution being initially of the same order as in ethanol, and changing gradually. Table 1 shows that with acetone this occurred only if a primary amino-group was present. *N*-Monoalkyl, *NN*-dialkyl, and *N*-acyl derivatives and salts of the amino-compounds (some measured in ethyl methyl ketone) gave maximal values immediately, as did proline ethyl ester, a cyclic amino-ester (cf. Johnson and McCaldin on interaction of proline with

TABLE 1.

	Amino-derivative	$[\alpha]_D$ in EtOH	Max. $[\alpha]_D^{22}$ ($\pm 3°$) in ketone
1	L-Alanine Et ester	+3° (*c* 3·94)	−130° (*c* 5·0) in $COMe_2$
2	D-Alanine Et ester	−2 (*c* 3·24)	+127 (*c* 3·48) ,,
3	L-Phenylalanine Et ester	+22 (*c* 3·1)	−125 (*c* 3·25) ,,
4	D-Phenylalanine Et ester	−22 (*c* 3·0)	+118 (*c* 3·0) ,,
5	L-Tyrosine Et ester	+18 (*c* 3·2)	−124 (*c* 4·12) ,,
6	L-Tyrosine amide	−23 (*c* 0·075)	−74 (*c* 0·086) in 1 : 1 (v/v) $COMe_2$–MeOH
7	(+)-Amphetamine	+33 (*c* 3·87)	+84 (*c* 4·66) in $COMe_2$
8	*N*-Methyl-L-tyrosine Me ester	+32 (*c* 1·44)	+24 (*c* 1·48) ,,
9	*NN*-Dimethyl-L-tyrosine Et ester	+38 (*c* 2·05)	+20 (*c* 2·14) ,,
10	*N*-Formyl-L-tyrosine Et ester	+37 (*c* 3·1)	+37 (*c* 2·21) in COMeEt
11	*N*-Phthaloyl-L-tyrosine Et ester	−196 (*c* 1·9)	−197 (*c* 2·32) ,,
12	L-Tyrosine Et ester hydrochloride	+25 (*c* 2·0)	+25 (*c* 2·19) in 3 : 22 (v/v) $COMe_2$–EtOH
13	L-Proline Et ester	−40 (*c* 2·1)	−25 (*c* 2·2) in $COMe_2$

• In MeOH.

ninhydrin [16]). The amino-esters containing a primary amino-group, on the other hand, required under our experimental conditions about 1—3 hours at 20—25° before they had their maximal rotation, which for all the amino-esters tested was of the same order of magnitude. L-Tyrosine amide, because of its insolubility in pure acetone, was measured in 1 : 1 acetone–methanol mixture, there requiring several days to reach its maximal rotation which was lower than those of the esters. For (+)-amphetamine also the increment was of a lower order.

The relatively high values of $[\alpha]$ obtained with the enantiomorphs of alanine and phenylalanine esters probably offer a means of determining the absolute configuration of α-amino-acid derivatives, although there are not yet sufficient examples for certainty. But combined with the procedure of Lutz and Jirgensons,[17] which consists of measuring polarimetrically α-amino-acids in hydrochloric acid (the rotatory power of L-α-amino-acids is displaced in a positive direction), esterification of α-amino-acids, followed by determination of their maximal rotation in a ketone, should help to decide their absolute configuration; those belonging to the L-series should be relatively highly lævorotatory and those of the D-series highly dextrorotatory. This might be particularly useful in the case of amino-acids with two asymmetric centres. To test this " rule," *p*-di-(2-chloroethyl)amino-L-phenylalanine ethyl ester (Melphalan ester) [18] was measured; the specific rotation in ethanol was +6·5° ± 1°, in acetone −68° ± 2°, and in *cyclo*pentanone −86° ± 2°. The ethyl esters of (+)- and (−)-α-amino-γ-[*p*-di-(2-chloroethyl)aminophenyl]-butyric acids [19,20] were also investigated; these compounds had been tentatively assigned, by Smith and Luck,[20] the D- and the L-configuration respectively on the basis of their anti-tumour activities and the greater activity of the L-phenylalanine homologue (Melphalan). The specific rotation value for the (+)-ester in ethanol was +23° ± 1° but in *cyclo*pentanone −70° ± 2°; that of the (−)-ester in ethanol was −26° ± 1°, but in *cyclo*pentanone +73° ± 2°; thus their absolute configurations appear to be the opposite

[16] Johnson and McCaldin, *J.*, 1958, 817.
[17] Lutz and Jirgensons, *Ber.*, 1930, **63**, 448.
[18] Bergel and Stock, *J.*, 1954, 2409.
[19] Davis, Roberts, and Ross, *ibid.*, 1955, 890.
[20] Smith and Luck, *J. Org. Chem.*, 1958, **23**, 837.

to those deduced from the biological results, a possibility already referred to by Smith and Luck [20] when taking into account their measurements in acid (Lutz–Jirgenson's rule [17]).

TABLE 2. *Maximal* $[\alpha]_D^t$.

Et ester from	*cyclo*Pentanone (*c* 3—3·25; *t* 19·5—24°)	*cyclo*Hexanone (*c* 3—4·24; *t* 22—24·5°)	Acetone (*c* 3—4·12; *t* 22—25·5°)	Et Me ketone (*c* 3—4·2; *t* 22—24°)	Et_2 ketone (*c* 3—3·25; *t* 18—24°)
L-Tyrosine	−161°	−127°	−124°	−107°	−40°
L-Phenylalanine...	−162	−142	−125	−103	−39
D-Phenylalanine...	+153	+137	+118	+106	+40

In Table 2 the effects of different ketones on the rotation of L-tyrosine and L- and D-phenylalanine esters are recorded. The values recorded are the highest obtained, *i.e.*, for dried solvents; lower values were sometimes encountered when operations were carried out under conditions of greater humidity in the laboratory. The magnitude of the maximal $[\alpha]_D$ decreases for all three esters from left to right in the Table. The times required for attainment of maximal rotation were 30—300 minutes, except for *cyclo*hexanone where it was only 4—10 minutes, although previously [15] it had been found that commercial samples of *cyclo*hexanone required up to 30 minutes.

The first question for consideration is whether the recorded maximal $[\alpha]_D$ refer to end products or to equilibrium mixtures (the sequence $COMe_2 > COMeEt > COEt_2$, for instance, would be accounted for if steric hindrance by the larger ethyl groups prevented completion of the reaction). A complete answer may require study of the concurrent changes in pH and the effect of temperature (cf. Hargreaves and Richardson [12]); a kinetic study is in progress by one of us (G. E. L.), but results already available and reported below permit preliminary conclusions.

As can be seen from Table 3, diluting acetone, *cyclo*hexanone, or *cyclo*pentanone solutions of tyrosine ethyl ester with ethanol caused a drop in the maximal rotatory power. Adding small amounts of water to acetone, either before or after dissolving the amino-ester

TABLE 3.

Ketone (% v/v)	Ethanol (% v/v)	Water (% v/v)	$[\alpha]_D^t$, *t*	Tyrosine Et ester (*c*)
Acetone				
12	88	—	−104°, 22°	4·0
96	—	4 *	−56·9,* 20	2·09
96	—	4	−54·5, 20	2·09
100	—	—	−124, 22	4·12
*cyclo*Pentanone				
50	50	—	−137, 21°	3·25
50	49	1	−132, 23·5	3·25
50	45	5	−117, 3·25	3·25
—	98·5	1·5	−18,† 24	4·5
100	—	—	−161, 19·5	3·25
*cyclo*Hexanone				
83·4	16·6	—	−119°, 22°	3·25
50	50	—	−118, 22·5	3·25
83·5	16	0·5	−111, 23	3·25
83·0	16	1·0	−101·5, 22·5	3·25
50	49	1·0	−105·5, 24	3·25
50	45	5·0	−66·5, 24	3·25
100	—	—	−127, 22	4·24

* Water added after the ester in dry acetone had been allowed to reach maximum rotation ($[\alpha]_D^{20}$ −126°), the value falling in 20 min. to the figure given.

† From the solid Schiff's base, initial $[\alpha]_D^{24}$ −101°, falling to above value in 140 hr.

in it, produced even greater diminution. The values for solutions in mixtures of *cyclo*hexanone or *cyclo*pentanone with ethanol and water were also lowered. For the acetone and *cyclo*pentanone mixtures, maximal values were reached only after longer times than with the undiluted ketones, but with *cyclo*hexanone under our conditions dilution had little effect on this time.

After solutions of tyrosine ester in aliphatic ketones (average *c* 3·0 to 4·0) had been left at 20—25° for long enough to reach their maximal specific rotation, adding 50—60 times their volume of light petroleum afforded crystalline precipitates, which for diethyl

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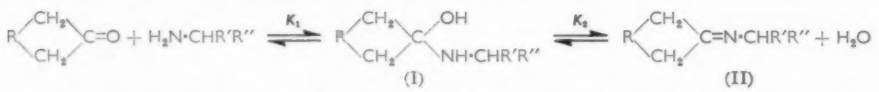
and ethyl methyl ketone represented 70—80% and for acetone *ca.* 50% of the quantity of the starting ester. This material consisted of L-tyrosine ethyl ester, characterised by m. p. and specific rotation ($+16° \pm 1°$). When higher concentrations of the ester in diethyl ketone and a smaller volume of light petroleum were used, the mother-liquor retained a small negative rotation, although the crystalline precipitate, $[\alpha]_D^{24\cdot5}$ $+15\cdot5° \pm 0\cdot5°$, represented nearly 97% of the starting ester. When these procedures were carried out with *cyclo*hexanone solutions, the precipitates were mostly oils but in some instances these were mixed with crystals; with larger amounts of light petroleum the precipitate had low dextrorotatory values, with smaller volumes of light petroleum $[\alpha]_D$ of the oil in ethanol had a distinct negative value which slowly diminished at 25°; the rotation of the mother-liquor was also negative.

*cyclo*Pentanone solutions gave with light petroleum a crystalline compound, $[\alpha]_D^{21}$ $-102° \pm 2°$ (*c* 2·0 in ethanol), whose analyses were correct for *N-cyclo*pentylidene-L-tyrosine ethyl ester (II; R = $[CH_2]_2$, R′ = *p*-HO·C_6H_4·CH_2, R″ = CO_2Et). This compound gave on hydrogenation *N-cyclo*pentyl-L-tyrosine ester, but did apparently not react with toluene-*p*-thiol, which has been reported to form adducts with Schiff's bases.[21] When it was left at 24° in ethanol–water ($[\alpha]_D^{24} = -101°$), its specific rotation fell in 140 hr. to −18° (see Table 3) and then precipitation with light petroleum afforded tyrosine ester. The infrared absorption spectrum of the *cyclo*pentylidene compound showed two double-bond frequencies, *viz.*, 1750 (ester C=O) and 1682 cm.$^{-1}$ (C=N, exocyclic to a five-membered ring [22]). Further infrared studies were carried out with *cyclo*hexanone and (+)-amphetamine, the latter being chosen because of the absence of the strongly absorbing ester group. *cyclo*Hexanone alone or mixed with various other solvents has a strong carbonyl absorption band near 1712 cm.$^{-1}$ (see Table 4, nos. 1—5; also Whiffen and Thompson [23]); amphetamine has two weak, primary amino-bands at 3358 and 3275 cm.$^{-1}$ (see Bellamy [24]) (these frequencies are somewhat higher for chloroform solutions; nos. 7 and 8). When the ketone and the amine were mixed in any proportion at 21° ± 3° the spectrum, initially the sum of those of the two compounds, rapidly changed: the strong band at 1712 cm.$^{-1}$ was replaced by one at 1655 cm.$^{-1}$ (cf. no. 6) of about half the intensity, and the two weak bands due to the amino-group were replaced by an intense broad band the position of which depended on the composition of the mixture (nos. 9—11).



(I) (II)

These results, together with our synthesis of the *cyclo*pentylidenetyrosine ester, indicated a reaction between *cyclo*hexanone and amphetamine with elimination of water, leading to the azomethine (II; R = $[CH_2]_3$, R′ = $PhCH_2$, R″ = Me) in solution. The band at 1655 cm.$^{-1}$ was then due to the formation of the C=N bond.[22] The new strong broad band was caused by the production of water, the variation in frequency being due to differences in hydrogen-bonding in the different mixtures; in fact absorption at 3550 cm.$^{-1}$ was also obtained on adding water to pure *cyclo*hexanone (no. 13). In a mixture of the ketone and amine (no. 10), the water formed, being present in a relatively large quantity, absorbed approximately like pure water, namely at 3350 cm.$^{-1}$; [25] the absorption was at 3450 cm.$^{-1}$ when the amine was in excess (no. 11) because the small proportion of water was bonded to the amine. To test this interpretation the effect of drying agents was studied. When anhydrous magnesium sulphate or calcium sulphate was added to various mixtures of ketone and amine, absorption in the 3200—3500 cm.$^{-1}$ region was

[21] Stacy, Day, and Morath, *J. Amer. Chem. Soc.*, 1955, **77**, 3869.
[22] Cf. Jones and Sandorfy in "Chemical Application of Spectroscopy," Vol. IX of "Technique of Organic Chemistry," ed. West, Interscience Publ. Inc., New York, 1956, p. 532.
[23] Whiffen and Thompson, *J.*, 1946, 1005.
[24] Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen and Co., London, 1954, p. 212.
[25] Gore, Barnes, and Peterson, *Analyt. Chem.*, 1949, **21**, 382.

reduced and the band near 1600 cm.$^{-1}$, where water also absorbs, disappeared. Removal of water might also be expected to change the equilibrium to give a greater concentration of azomethine (II); however, this was not proved, and for tyrosine ester and acetone (see Table 3) changes in rotation caused by addition of water could not be reversed simply by adding calcium sulphate.

Discussion and Conclusions.—Most of the azomethines described in the literature are formed from amino- and carbonyl compounds when at least one component contains an aromatic ring or the carbonyl group is that of an aldehyde. However, azomethines from ketones and non-aromatic amines are known, *e.g.*, Bergmann *et al.*[26] reported the preparation of such compounds from β-hydroxy-amines, and Witkop [27] discussed the properties of a Schiff's base from *cyclo*hexanone and *cyclo*hexylamine. Production of azomethines from amino-esters and aromatic aldehydes has been described by Velluz *et al.*,[28] Bergel and Cohen,[29] and Pfeiffer, Offermann, and Werner.[30] One could assume that analogous substances have been formed between amino-acids and carbonyl compounds in a number of reactions mentioned above. But in no case, to our knowledge, has the isolation of a simple condensation product from ketones been reported, at least not under our mild conditions.

Ingold [31] considered it plausible that H–N addition to carbonyl groups should commence with formation of amino-alcohols (I) which, in the case of primary amino-compounds, is followed by dehydration to the azomethines (II). This sequence is supported by our observations, and especially by the infrared measurements for *cyclo*hexanone–amphetamine. Here it is likely that the equilibrium constant K_2 for formation of the azomethine (II) and water is greater than K_1, as dilution of the mixture with chloroform rapidly regenerated the starting compounds, and the amino-alcohol (I), whose concentration at any time must have been very small, could not be detected. The difference in rate of reaction of tyrosine ester with *cyclo*hexanone and *cyclo*pentanone, and the stabilities of the azomethines formed, could be explained in terms of the strain theory [see Bellamy [24] (p. 128); and Brown, Brewster, and Shechter [32]] which postulates that the six-membered ring is less strained in a *cyclo*hexyl derivative than in a *cyclo*hexylidene compound while the reverse is true of the five-membered ring. Hence one could expect that *cyclo*hexanone would form an amino-alcohol, and hence an azomethine, more rapidly than would *cyclo*pentanone, but that the Schiff's base from the latter, once formed, would be more stable than that from the former. Moreover, in the case of the azomethine from *cyclo*hexanone the existence of an equilibrium between the C=N compound and an enamine tautomer (see Witkop [27]) might add further complications.

Experimental

Optical Rotations.—Measurements were for the sodium D line, with a 1 dm. polarimeter tube. A weighed amount of the amino-compound was dissolved in the ketone (2 ml.) or in the mixture of ketone with other solvents. The time of addition of the ketone was taken as zero time, and the first readings were taken usually about three minutes later.

Solvents.—Ethanol was boiled with sodium under reflux with diethyl phthalate and then distilled through a short column.[33]

Before polarimetry the ketones were warmed with small amounts of potassium permanganate until a permanent pink colour remained, dried (K_2CO_3; sometimes under reflux), and distilled through a short fractionating column. For the infrared measurements, *cyclo*hexanone was purified by formation of the bisulphite compound, which was washed with ethanol followed by

[26] Bergmann, Zimkin, and Pinchas, *Rec. Trav. chim.*, 1952, **71**, 186.
[27] Witkop, *J. Amer. Chem. Soc.*, 1956, **78**, 2873.
[28] Velluz, Amiard, and Heymès, *Bull. Soc. chim. France*, 1954, 1012.
[29] Bergel and Cohen, B.P. 556,044/1943.
[30] Pfeiffer, Offermann, and Werner, *J. prakt. Chem.*, 1942, **159**, 313.
[31] Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, Ithaca, 1953, p. 687.
[32] Brown, Brewster, and Shechter, *J. Amer. Chem. Soc.*, 1954, **76**, 467.
[33] See Vogel, "Practical Organic Chemistry," Longmans, Green and Co., London, 1954, p. 166.

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considerable amounts of ether to remove *cyclo*hexanol and then decomposed with 2N-sodium carbonate which was extracted with ether.

Amino-esters and Related Substances.—L-Tyrosine ethyl ester was either prepared in the usual manner from L-tyrosine or purchased from Kodak Ltd. and recrystallised from ethyl acetate.

Other amino-esters were obtained by refluxing the corresponding amino-acids in ethanolic hydrogen chloride. After removal of the solvent, the residual ester hydrochloride was treated with aqueous sodium carbonate or with triethylamine. In the former case the aqueous solution was extracted with ethyl acetate: after drying (Na_2SO_4), the solvent was removed *in vacuo*. In the latter case, the hydrochloride, dissolved or suspended in a small volume of ethanol-free chloroform, was treated with one equivalent of triethylamine, and the triethylamine hydrochloride precipitated by the addition of 5—10 volumes of dry ether. The solution was filtered and the solvent removed *in vacuo*. The free amino-esters were liberated from the hydrochloride only as required, to obviate dioxopiperazine formation.

NN-Dimethyl-L-tyrosine was prepared by reductive alkylation of L-tyrosine in the presence of formaldehyde.[34]

N-Methyl-L-tyrosine methyl ester was prepared by reductive alkylation of L-tyrosine methyl ester in methanol with one equivalent of aqueous formaldehyde.[34]

L-Tyrosine amide was prepared by the technique of Koenigs and Mylo.[35]

(+)-Amphetamine was prepared from the commercial sulphate by the method used for the amino-ester hydrochlorides.

Melphalan ethyl ester hydrochloride was prepared by Dr. J. A. Stock by treatment of Melphalan (CB 3025) with ethanolic hydrogen chloride at 5°; recrystallised from chloroform–ethanol, it had m. p. 165—167°.[36]

(+)- and (−)-α-Amino-γ-(*p*-di-2-chloroethylaminophenyl)butyric acid, kindly supplied by Professor J. M. Luck and Dr. H. E. Smith,[20] were esterified by Dr. J. A. Stock with saturated ethanolic hydrogen chloride at 24°. The ester hydrochlorides were precipitated with absolute ether as gums and, without further purification, submitted to paper-chromatography [Whatman No. 1 paper; butanol–ethanol–propionic acid–H_2O (10 : 5 : 2 : 5)] which showed them to be essentially homogeneous (R_F 0·88). The gums were transformed into the ester bases by treatment with aqueous sodium hydrogen carbonate and extraction with ethyl acetate. The dried oily residues from this solvent were then used for polarimetric measurements:

p-Di-2-chloroethylamino-L-phenylalanine ethyl ester, $[\alpha]_D^{24}$ +6·5° ± 1° (*c* 1·65 in ethanol), $[\alpha]_D^{24}$ −68° ± 2° (*c* 3·0 in acetone), $[\alpha]_D^{19}$ −86° ± 2° (*c* 2·4 in *cyclo*pentanone, after *ca.* 4 hr.).

Ethyl (+)-α-amino-γ-(*p*-di-2-chloroethylaminophenyl)butyrate, $[\alpha]_D^{24}$ +23° ± 1° (*c* 2·75 in ethanol), $[\alpha]_D^{24}$ −70° ± 2° (*c* 2·7 in *cyclo*pentanone, after *ca.* 2 hr.); lævorotatory isomer, $[\alpha]_D^{24}$ −26° ± 1° (*c* 2·85 in ethanol), $[\alpha]_D^{24}$ +73° ± 2° (*c* 2·85 in *cyclo*pentanone).

Precipitation of Ketonic Solutions with Light Petroleum.—To the solution of tyrosine ethyl ester in the ketone (approx. 2 ml.), remaining after polarimetric measurements had been completed, light petroleum (100—120 ml.) was added. The mixture was left at 0° overnight, and the precipitated crystals were filtered off and their melting point and rotation measured. The rotation of the mother-liquors was also measured, but was very low.

From ester (81 mg.) and acetone (2 ml.), crystals (42·9 mg., 53%) were isolated, having m. p. 98—104°, $[\alpha]_D^{24}$ +15·6° (*c* 2·37 in ethanol).

From ester (79·5 mg.) and ethyl methyl ketone (2 ml.), crystals (60 mg., 76%) were isolated, of m. p. 101—105°, $[\alpha]_D^{26}$ +16·3° (*c* 3·0 in ethanol).

From ester (80·3 mg.) and diethyl ketone (2 ml.), crystals (61·9 mg., 78%) were isolated, having m. p. 102—105°, $[\alpha]_D^{26}$ +16·5° (*c* 3·1 in ethanol).

From ester (65 mg.) and *cyclo*pentanone (2 ml.), crystals (47·4 mg., 73%) were isolated, having m. p. 115—129° (decomp.), $[\alpha]_D^{20}$ −100° (*c* 2·37 in ethanol) (see below).

From ester (80 mg.) and *cyclo*hexanone (2 ml.), oily material, $[\alpha]_D^{23}$ +5° (*c* 1·3 in ethanol) (18 mg., 23%), was produced.

The ester (120 mg.) was dissolved in diethyl ketone (1 ml.) which was mixed with light petroleum (24 ml.) and after 5 hr. at 0° the solution was decanted from the crystals {116 mg., 96·6%; $[\alpha]_D^{24.5}$ +15·5° (*c* 5·8 in ethanol)} and an aliquot part (*ca.* 1 ml.) was assayed polarimetrically (α − 0·03° ± 0·005°).

[34] Bowman and Stroud, *J.*, 1950, 1342.
[35] Koenigs and Mylo, *Ber.*, 1908, **41**, 4441.
[36] Personal communication.

To the ester (120 mg.) in *cyclo*hexanone (1 ml.) was added light petroleum (24 ml.). The turbid solution was left at 0° for *ca.* 3 hr., an oil and a few crystals being precipitated {122·7 mg.; $[\alpha]_D^{22\cdot5}$ −48° ± 1° (*c* 6·135 in ethanol), slowly diminishing}. The solution decanted from the oil had α − 0·055°. If the precipitate was a 1 : 1 mixture of *cyclo*hexylidene-L-tyrosine ethyl ester and the starting ester, the specific rotation (*c* 0·07 in light petroleum–*cyclo*hexanone) was $[\alpha]_D^{23}$ −78·0° ± 2°.

N-cyclo*Pentylidene-L-tyrosine Ethyl Ester*.—Saturation of *cyclo*pentanone (5 ml.) with L-tyrosine ethyl ester (1·0 g.) at 20° gave after a few minutes a precipitate of colourless crystals (70%) which were washed with ether. The yield was increased by adding light petroleum to the mother-liquors which, like other solutions of this compound, became gradually yellow. Recrystallisation from *cyclo*pentanone–light petroleum (b. p. 100—120°) gave material of m. p. 132° (decomp.), $[\alpha]_D^{21}$ −102° (*c* 2·0 in EtOH) (Found: C, 69·6; H, 7·6; N, 5·1. $C_{16}H_{21}O_3N$ requires C, 69·8; H, 7·7; N, 5·1%). This N-cyclo***pentylidene-L-tyrosine ethyl ester*** was slowly degraded to tyrosine ester in ethanol–water (98·5 : 1·5).

Hydrogenation in ethanol with platinum black, addition of dilute aqueous hydrochloric acid, and removal of the solvent *in vacuo* gave a colourless solid which was precipitated from ethanol by ether as needles of N-cyclo***pentyl-L-tyrosine ethyl ester hydrochloride***, m. p. 208—209°, $[\alpha]_D^{24}$ +33·5° (*c* 2·0 in ethanol) (Found: N, 4·5; Cl, 12·0. $C_{16}H_{24}O_3NCl$ requires N, 4·5; Cl, 11·3%).

The free *amino-ester* was liberated by aqueous sodium hydrogen carbonate; recrystallised from ethyl acetate–light petroleum, it had m. p. 138—139° (mixed m. p. with the *cyclo*pentylidene compound 110—115°), $[\alpha]_D^{24}$ −1·5° (*c* 2·0 in ethanol) (Found: C, 68·8; H, 8·35; N, 5·0. $C_{16}H_{23}O_3N$ requires C, 69·3; H, 8·4; N, 5·05%).

TABLE 4. *Frequencies of infrared bands.*

No.	*cyclo*Hexanone (%)	Amphetamine (%)	Other solvent (% v/v)	ν (cm.$^{-1}$)
1	100	—	—	1712
2	5	—	CCl_4 95	1717
3	5	—	$CHCl_3$ 95	1705
4	5	—	C_6H_{13}·CHMe·OH 95	1708
5	5	—	NH_2Ph 95	1702
6	5	95	—	1710, 1655
7	—	100	—	3358, 3275
8	—	5	$CHCl_3$ 95	3368, 3297
9	90	10	—	*ca.* 3550
10	50	50	—	*ca.* 3350
11	10	90	—	*ca.* 3450
12	—	—	H_2O 0·15, in $CHCl_3$ 99·85	3681, 3603
13	90	—	H_2O 10	3550
14	—	—	C_6H_{13}·CHMe·OH 100	3350
15	—	—	C_6H_{13}·CHMe·OH 10 $CHCl_3$ 90%	3610, 3440
16	90	—	C_6H_{13}·CHMe·OH 10	3495

Infrared Absorption Measurements (see Table 4).—The *cyclo*hexanone–amphetamine experiments were carried out on a Perkin-Elmer Model 12C spectrometer, with a sodium chloride prism for the carbonyl band measurements and a lithium fluoride prism for those at 3000 cm.$^{-1}$. Pure *cyclo*hexanone was measured as a capillary film, and all other measurements were made in sealed cells of either 33 or 100 μ thickness. The chloroform used was washed with water, dried, and stored in a dark bottle.

Measurements of the *cyclo*pentylidene compound were made with a Perkin-Elmer Infracord spectrophotometer (sodium chloride prism), the sample being in a mull with liquid paraffin.

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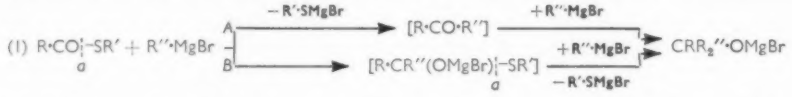
280. *Thioacids. Part II.* Action of Arylmagnesium Halides on Aromatic Thiol-acids.*

By Mohamed A. Elkaschef, Michael H. Nosseir, and Kamal El-Din Mokhtar.

Aromatic thiol-acids with arylmagnesium halides give, through elimination at the carbon–oxygen bond, triarylmethanethiols, in contrast to the triarylmethanols obtained from the same reagent and aromatic thiol-esters through elimination at the carbon–sulphur bond. A new condensation is described between bromomagnesium salts of aromatic thiol-acids and bromomagnesium derivatives of triaryl-methanols or -methanethiols on decomposition in sulphuric acid, to give triaryl esters or thiol-esters respectively.

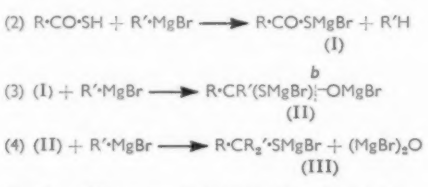
In agreement with Hepworth and Clapham [1] and Gilman *et al.*[2] we found that 3 mol. of phenylmagnesium bromide react with 1 mol. of phenyl or naphthyl thiolbenzoate to give triphenylmethanol. The course of reaction (*A* or *B*) could not be decided as treatment of



naphthyl thiolbenzoate with 1 equiv. of phenylmagnesium bromide had no effect, but essentially elimination takes place at the carbon–sulphur link (*a*).

Moreover, as Grignard found,[3] triphenylmethanol was obtained from 3 mol. of phenylmagnesium bromide and 1 mol. of benzoic acid. The reaction can be represented by the reaction 1, with OMgBr replacing SR′.

Grignard reagents react differently with aromatic thiol-acids; 3 mol. of phenyl- or *p*-tolyl-magnesium bromide and 1 mol. of thiolbenzoic acid afford triphenylmethyl or phenyldi-*p*-tolylmethyl thiolbenzoate respectively on acid decomposition of the magnesium complexes. Decomposition with ammonium chloride followed by ether extraction gave triphenylmethanol (thiol changing to alcohol during decomposition) from the ethereal layer and the starting thiol-acid from the aqueous layer; this eliminates interaction between the products. We thus assume that, on acid decomposition, condensation takes place between the residual bromomagnesium salt of the thiol-acid (I) and the formed bromomagnesium derivative of the triarylmethanethiol (III):



Evidence favouring this mechanism was sought as follows. While the free thiolbenzoic acid and triphenylmethanethiol do not condense, their bromomagnesium derivatives (I) and (III) readily do so to give the triarylmethyl thiolbenzoate (IV) with evolution of

* The paper, *J.*, 1958, 2893, is considered to be Part I.

[1] Hepworth and Clapham, *J.*, 1921, **119**, 1188.
[2] Gilman, Robinson, and Beaber, *J. Amer. Chem. Soc.*, 1926, **48**, 2715.
[3] Grignard, *Compt. rend.*, 1904, **138**, 152.

hydrogen sulphide (reaction 5) when poured into dilute sulphuric acid and treated in the usual manner.

This new type of reaction also occurs between the bromomagnesium derivatives of thiolbenzoic acid and triphenylmethanol to give triphenylmethyl benzoate:

$$(6)\ R'\cdot\overset{O}{\overset{\|}{C}}\cdot SMgBr + R_3C\cdot OMgBr \longrightarrow R'\cdot CO\cdot O\cdot CR_3 + (MgBr)_2S$$

but not between the bromomagnesium derivatives of benzoic acid and triphenylmethanol or triphenylmethanethiol. The thiol-acid, necessary to this reaction, loses its sulphur atom: accordingly, the sulphur atom in the *S*-triarylmethyl esters formed must come from the triarylmethanethiols first formed by an elimination (reaction 4) at the carbon–oxygen link (*b*, reaction 3) in contrast to that at the carbon–sulphur link of thiol-esters.

p-Methoxyphenylmagnesium bromide (3 mol.), with thiolbenzoic acid (1 mol.), however, gives dibenzoyl disulphide on decomposition of the magnesium complex. This reaction cannot be a condensation of two molecules of the bromomagnesium salt of the thiol-acid, as the pure salt gave benzoic acid on the same treatment, even in presence of anisole added to simulate the conditions of the principal reaction. Also, it cannot be due to oxidation as this did not occur in other Grignard reactions under the same conditions. Since we get the same result with either method of decomposition, the disulphide ought to have been formed before decomposition. Therefore, the disulphide is likely to have been formed through the formation of free radicals under the influence of the *p*-methoxyphenylmagnesium bromide. In like manner the action of phenylmagnesium bromide on *p*-chlorothiolbenzoic acid, giving bis-(*p*-chlorobenzoyl) disulphide, can be explained. As the *p*-methoxymagnesium bromide contains an electron-donating group and *p*-chlorothiolbenzoic acid an electron-attracting atom in the *para*-positions, these reactions would be expected to follow the same course.

Experimental

Yields are mostly of pure products; low yields are due to losses in reaction and to the inefficiency of the method of separation.

Action of Phenylmagnesium Bromide (3 *Mols.*) *on Phenyl Thiolbenzoate* (1 *Mol.*).—A cold solution of phenylmagnesium bromide [from bromobenzene (3·2 c.c.)] in ether (40 c.c.) was added to a cold solution of phenyl thiolbenzoate (2·1 g.) in benzene (20 c.c.). Next day the mixture was refluxed for 2 hr., then poured into water (250 c.c.), concentrated sulphuric acid (2·5 c.c.), and crushed ice (30 g.). The organic layer and the ethereal extract were united, washed, and dried (Na_2SO_4), and on evaporation of the solvents gave a solid (1 g.), which (from light petroleum, b. p. 60—90°) afforded triphenylmethanol, m. p. and mixed m. p. (cf. ref. 4) 163°.

Action of Phenylmagnesium Bromide (3 *Mol.*) *on Naphthyl Thiolbenzoate* (1 *Mol.*).—As above, naphthyl thiolbenzoate (cf. ref. 5) (2·6 g.) gave triphenylmethanol (0·8 g.), m. p. and mixed m. p. 163°. Using only 1 mol. of phenylmagnesium bromide, we recovered the starting materials.

Phenylmagnesium Bromide (3 *Mol.*) *and Benzoic Acid* (1 *Mol.*).—Benzoic acid (1·2 g.) in a reaction as above afforded a solid from the ethereal layer. This, on fractional crystallisation from light petroleum (b. p. 60—90°), gave triphenylmethanol (0·25 g.), m. p. and mixed m. p. 163°, and benzoic acid, m. p. 121° (from water).

Phenylmagnesium Bromide (3 *Mol.*) *and Thiolbenzoic Acid* (1 *Mol.*).—(i) In a reaction as before, with thiolbenzoic acid (cf. ref. 6) (1·5 g.) in ether and phenylmagnesium bromide [from bromobenzene (3·2 c.c.)], the residue, isolated with ether, on fractional crystallisation from light petroleum (b. p. 70—80°) afforded triphenylmethanol (0·3 g.), m. p. and mixed m. p. 163°, and triphenylmethyl thiolbenzoate (0·7 g.), m. p. and mixed m. p. (cf. ref. 7) 188°.

(ii) Reaction as above, but decomposition with ammonium chloride and ice, gave triphenylmethanol from the ethereal layer and thiolbenzoic acid from the aqueous layer.

[4] Acree, *Ber.*, 1904, **37**, 2755.
[5] Taboury, *Compt. rend.*, 1904, **138**, 983.
[6] Kym, *Ber.*, 1899, **32**, 3533.
[7] Elkaschef and Nosseir, *J.*, 1958, 2893.

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Triphenylmethanethiol treated with phenylmagnesium bromide and decomposed with ammonium chloride gave triphenylmethanol.

p-*Tolylmagnesium Bromide* (3 *Mol.*) *and Thiolbenzoic Acid* (1 *Mol.*).—Thiolbenzoic acid (4·2 g.) and *p*-tolylmagnesium bromide [from *p*-bromotoluene (11·4 g.)], as above, with 4 hours' reflux and decomposition with sulphuric acid, afforded *phenyl di*-p-*tolylmethyl thiolbenzoate* from the ethereal layer as an oil that solidified under methanol. It gave colourless crystals (2·0 g.) m. p. 136°, from ethanol, giving yellowish-brown colours with concentrated sulphuric acid (Found: C, 82·3; H, 5·8; S, 7·9. $C_{28}H_{24}OS$ requires C, 82·3; H, 5·9; S, 7·8%). To this ester (0·3 g.) in boiling acetic acid (20 c.c.) containing 1 c.c. of concentrated hydrochloric acid, zinc powder (activated with copper sulphate) (0·7 g.) was added, and the mixture poured into water. Isolation with ether afforded phenyldi-*p*-tolylmethane, m. p. and mixed m. p. (cf. ref. 8) 54°.

Condensations.—(a) *Bromomagnesium thiolbenzoate and triphenylmethanethiol bromomagnesium derivative.* Bromomagnesium thiolbenzoate [from phenylmagnesium bromide (from 1·1 c.c. of bromobenzene) and thiolbenzoic acid (1·4 g.) refluxed in dry ether for 2 hr.] and the bromomagnesium derivative of triphenylmethanethiol [from phenylmagnesium bromide as before and triphenylmethanethiol (cf. ref. 9) (2·7 g.) refluxed in ether for 2 hr.] were mixed, left overnight, and refluxed for 1 hr. After decomposition with dilute sulphuric acid, the oil isolated with ether solidified under light petroleum (b. p. 60—90°) on cooling. Recrystallised from light petroleum (b. p. 100—120°), triphenylmethyl thiolbenzoate (1·2 g.) had m. p. and mixed m. p. (cf. ref. 7) 188°.

Ethereal thiolbenzoic acid and triphenylmethanethiol, in equimolecular quantities, when heated for 1 hr., poured into cold dilute sulphuric acid, and treated as above, afforded the starting substances.

(b) *Bromomagnesium thiolbenzoate and triphenylmethanol bromomagnesium derivative.* Similarly, triphenylmethanol (2·6 g.) gave a solid from the ethereal layer. After being boiled with light petroleum (b. p. 60—90°), the part that dissolved gave on cooling and recrystallisation from benzene triphenylmethyl benzoate (0·1 g.), m. p. and mixed m. p. (cf. ref. 10) 166°; the insoluble part, recrystallised from the same light petroleum, afforded triphenylmethanol (0·4 g.), m. p. 163°.

(c) *Bromomagnesium benzoate and triphenylmethanethiol bromomagnesium derivative.* Using triphenylmethanethiol (13·8 g.) and benzoic acid (6·1 g.) as in (a), we got back the starting materials.

Action of p-*Methoxyphenylmagnesium Bromide* (3 *Mol.*) *on Thiolbenzoic Acid.*—Thiolbenzoic acid (4·2 g.) and a Grignard reagent (from 11·4 c.c. of *p*-bromoanisole) in a reaction as before with 4 hours' boiling and decomposition with either sulphuric acid or ammonium chloride, gave dibenzoyl disulphide (1·0 g.), m. p. and mixed m. p. (cf. ref. 11) 132°.

Bromomagnesium thiolbenzoate prepared from equimolar amounts of thiolbenzoic acid and methylmagnesium iodide gave, after the usual treatment, benzoic acid, m. p. 121°, together with much resin.

A similar bromomagnesium salt of thiolbenzoic acid (from ethylmagnesium bromide) in ether was refluxed for 4 hr. in presence of 1 equiv. of anisole. After treatment as before benzoic acid was obtained together with much resin.

Action of Phenylmagnesium Bromide (3 *Mol.*) *on* p-*Chlorothiolbenzoic acid* (1 *Mol.*).—Reaction of *p*-chlorothiolbenzoic acid (1 g.) in dry benzene and a Grignard reagent [from bromobenzene (1·8 c.c.)] with 4 hours' boiling and decomposition with sulphuric acid, gave bis-(*p*-chlorobenzoyl) disulphide as an oil from the ethereal layer. It solidified under ethanol and, crystallised therefrom (0·25 g.). had m. p. and mixed m. p. (cf. below) 127°.

Preparation of p-*Chlorothiolbenzoic Acid.*—*p*-Chlorobenzoyl chloride [12] (13·0 g.) was added in portions to a solution of potassium hydrogen sulphide in ethanol (from 13 g. of potassium hydroxide in ethanol saturated with hydrogen sulphide) with cooling and passage of hydrogen sulphide. Most of the alcohol was distilled off. The solution was acidified with hydrochloric acid, filtered, diluted with water, and extracted with ether. The ethereal extract, washed, dried (Na_2SO_4), and evaporated, gave p-*chlorothiolbenzoic acid* (13·0 g.) Crystallised from dry

[8] Kliegl, *Ber.*, 1905, **38**, 84.
[9] Vörlander and Mittag, *Ber.*, 1913, **46**, 3453.
[10] Wieland, Ploetz, and Indest, *Annalen*, 1937, **532**, 186.
[11] Schelton and Rider, *J. Amer. Chem. Soc.*, 1936, **58**, 1282.
[12] Meyer, *Monatsh.*, 1901, **22**, 778.

light petroleum (b. p. 70—80°), it had m. p. 187—188° (Found: C, 48·7; H, 2·3. C_7H_5OSCl requires C, 48·7; H, 2·8%).

Preparation of Bis-(p-chlorobenzoyl) Disulphide.—Crystalline sodium disulphide (5 g.) was added to a solution of *p*-chlorobenzoyl chloride (5 g.) in acetone (20 c.c.), containing anhydrous sodium sulphate (3 g.) The mixture was reflxued for 1 hr., allowed to cool, then diluted with water and made alkaline with sodium hydroxide. The precipitate was filtered off, and washed with water. *Bis-(p-chlorobenzoyl) disulphide* (5 g.) thus obtained crystallised from methanol or light petroleum (b. p. 100—110°) in crystals, m. p. 127°; it becomes red at 190° (Found: C, 48·9; H, 2·5; S, 19·4; Cl, 20·4. $C_{14}H_8O_2S_2Cl_2$ requires C, 49·0; H, 2·3; S, 18·7; Cl, 20·7%).

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281. *Chemical Constitution and the Dissociation Constants of Monocarboxylic Acids. Part XVIII.* Some Acetic and Propionic Acids Substituted with Hydrocarbon Radicals in 10% and 25% (w/w) Acetone–Water Solutions.*

By J. F. J. DIPPY, S. R. C. HUGHES, and A. ROZANSKI.

The thermodynamic dissociation constants of a series of acetic and propionic acids progressively substituted with alkyl and phenyl groups have been measured conductimetrically in 10% and 25% (w/w) acetone–water solutions at 25°. Steric effects on ionisation were studied by plotting (i) log K against the reciprocal of the dielectric constant of the solvent (including data for aqueous solutions), and (ii) log K in the first solvent against log K in the second. Acetic acids substituted with two or more bulky groups are weakened by lowering the solvent dielectric constant appreciably more than are similar β-substituted propionic acids and monosubstituted acetic acids; this is attributed to steric inhibition of solvation. Unexpectedly, acetic acid, and probably propionic acid also, show behaviour different from that of other acids free from steric effects, and this cannot be simply explained.

THERE are few results for the dissociation constants of carboxylic acids in non-aqueous and partially aqueous solvents, although they have been accumulating.[1] The relative change of strength of an acid in different solvents is governed by the basicity and dielectric constant of the solvent, and by any specific solvent–solute interactions which affect ionisation. It is generally held [2] that the sequence of strengths of acids in which the substituents do not exert appreciable spatial effects on the proton transfer site is the same in different solvents; where, however, such effects exist different sequences may be observed in different solvents (*e.g.*, *ortho*-substituted benzoic acids). Furthermore, provided that the solvents are constitutionally similar it is possible to apply the well-known correlation log $K \propto 1/D$ (D = dielectric constant) [3] (generally for $D > 25$). It follows that for acids free from any steric effect the slopes of the lines in the log K *versus* $1/D$ plot are almost identical, and that a plot of log K' (in one solvent) against log K'' (in a second solvent) should be a straight line with unit slope; for sterically-hindered acids, plots of log K against $1/D$ have varying slopes, and the points do not fall on a straight line in the log K' *versus* log K'' plot.[5,6] The present investigation was carried out to supply

* Part XVII, *J.*, 1957, 2405.

[1] Izmailov, *Zhur. fiz. Khim.*, 1950, **24**, 321.
[2] Ingold, "Structure and Mechanism in Organic Chemistry," Bell & Sons, London, 1953.
[3] Wynne-Jones, *Proc. Roy. Soc.*, 1933, *A*, **140**, 440.
[4] Kilpatrick, *Chem. Rev.*, 1933, **13**, 136.
[5] Dippy and Davey, *J.*, 1944, 411.
[6] Wooten and Hammett, *J. Amer. Chem. Soc.*, 1935, **57**, 2289.

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more evidence for the above feature, and to determine whether a study of acid strengths in chemically similar solvents could distinguish between acids whose electrolytic dissociation is determined solely by polar effects, and those in which steric effects play a substantial, additional rôle.

The mean values of the thermodynamic dissociation constants in aqueous acetone solutions determined by the authors, and those from the literature for aqueous solutions, are shown in Table 1.

Aqueous acetone was chosen as a compromise between the solubility requirements of some of these acids and the theoretical and practical difficulties accompanying measurements in pure non-aqueous solvents. The basicities of these solvents (as measured by the acidity function, H_0, interpolated from the Braude's results [7]) are given in Table 2; this trend, combined with the decrease in dielectric constant of the solvent as the percentage of acetone increases, progressively lowers the acid strengths.

TABLE 1. *Mean values of thermodynamic dissociation constants* (10^5K *at* 25°) *and melting or boiling points.*

Acid	10% Acetone–water	25% Acetone–water	Water *	$-\Delta \log K/\Delta 1/D$ (mean)	M. p.	M. p. (lit.) ‡
Acetic	1·25	0·585	1·75 [a]	160·0	118° †	118·1°
Propionic	1·03	0·363	1·34 [b]	176·0	141 †	141·1
Trimethylacetic	0·586	0·162	0·891 [a]	238·0	274	265
β-Phenylpropionic	1·26	0·403	2·19 [c]	251·0	50	49·5
Phenylacetic	2·71	0·861	4·88 [d]	259·0	76·5	76
Benzoic	3·52	1·01	6·27,[e] 6·53 [f]	279·0	122·2	122
ββ-Dimethyl-β-phenylpropionic	0·536	0·154	—	281·0	60	58·5
ββ-Diphenylpropionic	1·48	0·420	—	284·0	155·2	155
Methylneopentyl-t-butylacetic (Siccatic B)	0·0680	0·0151	—	339·0	132—132·5	130
Diphenylacetic	4·76	0·958	11·5 [d]	376·0	148·5	148
Triphenylacetic	4·26	0·802	—	376·0	274	265
Dineopentylacetic (Siccatic A)	0·384	0·0667	—	394·0	86·5—87	55

* Best conductimetric values from literature. † B. p. at 769 mm. Trimethylacetic acid had b. p. 118°/769 mm. (lit. 118·1°). ‡ Best value from literature.

[a] Dippy, *J.*, 1938, 1222. [d] Dippy and Williams, *J.*, 1934, 161. [b] Belcher, *J. Amer. Chem. Soc.*, 1938, **60**, 2744. [c] Dippy and Lewis, *J.*, 1937, 1008. [e] Dippy and Williams, *J.*, 1934, 1888. [f] Ives, *J.*, 1933, 561.

TABLE 2. *Acidity functions,* H_0, *for aqueous acetone solutions* (*from Braude* [7]).

	H_0		
	Water	10% Acetone–water	25% Acetone–water
0·1M-HCl	1·01	1·14	1·41
1M-HCl	−0·33	−0·12	0·28

The plot of log K against $1/D$ (Fig. 1) shows that, where the values of K in the three media are available, good straight lines are obtained (trimethylacetic and propionic acids showing the poorest correlations). The acids fall into three groups as regards the relative magnitudes of the slopes: (i) monosubstituted acetic acids, trimethylacetic acid, and mono-, di-, and tri-β-substituted propionic acids (and benzoic acid as reference), (ii) di- and tri-substituted acetic acids (except trimethylacetic), and (iii) acetic acid. In the plot of log K' against log K'' the first group lies approximately on a straight line of unit slope, whilst the points representing the acids of the second group are above this line and those for acetic acid (and propionic acid in water) fall below it (Figs. 2 and 3). This classification shows that considerations of the size of the substituent and its distance from the carboxyl group govern qualitatively the behaviour of these acids in the solvents. Both small and large substituents in the β-position influence the relative change of strengths in aqueous acetone in the same degree as a single substituent in acetic acid. On the other hand, two

[7] Braude, *J.*, 1948, 1976.

or three bulky substituents (phenyl, neopentyl, and t-butyl, but not methyl) on the α-carbon atom sharply decrease the relative strength in aqueous acetone (exhibited by steeper slopes in Fig. 1), *e.g.*, triphenylacetic and siccatic acids show unusually large depression of strength in these solvents (cf. ref. 8). The primary steric effect must be considered to operate here. The energy of solution of the carboxylate ion is greater than that of the undissociated acid molecule, so steric compression of the carboxyl group in hindered acids preferentially inhibits solvation of the anion, thus diminishing the ionic

FIGS. 1—3. For key to numbers see Table 4.

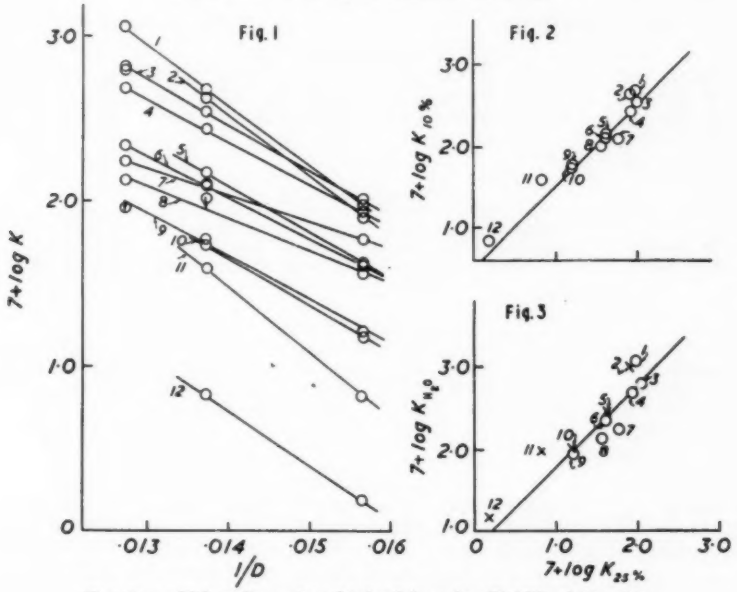

FIG. 3, × Values for water obtained from log K–1/D relationship.

concentration in the dissociation equilibrium, *i.e.*, acid strength falls. This effect becomes more marked as the percentage of acetone in the solvent increases, *i.e.*, as anion solvation becomes increasingly difficult.

With acetic acid and, probably, propionic acid, factors apparently operate which produce an effect opposite to that created when bulky substituents compress the carboxyl group (Figs. 2 and 3). It is possible that, owing to the relatively small size of these molecules, some specific interactions, easily influenced by the nature of the solvent, occur, but it is difficult to speculate as to their nature.

This work emphasises the view that a comparison of monocarboxylic acid strengths in two or more related solvents furnishes a criterion of the operation of steric factors in the dissociation of carboxylic acids, and this method of comparison may be applicable to other acid systems to differentiate between the diverse steric factors.

EXPERIMENTAL

Preparation and Purification of Acids.—Triphenylacetic acid (from Dr. Weedon of Imperial College, London) and siccatic acids A and B (from Alchemy Ltd.) were gifts which we gratefully acknowledge. ββ-Diphenylpropionic and ββ-dimethyl-β-phenylpropionic acids were prepared

[8] Hammond and Hoyle, *J. Amer. Chem. Soc.*, 1955, **77**, 338; Kilpatrick and Fachenthal, *J. Electrochem. Soc.*, 1953, **100**, 185.

TABLE 3. *Physical constants of the solvents.*

	d_4^{25}	η_0^{25}	D_{25} * (H_2O = 78·6)
10% (w/w) Acetone–water	0·9832	0·01105	73·0
25% (w/w) Acetone–water	0·9618	0·01335	64·0

* From Harned and Owen, " Physical Chemistry of Electrolyte Solutions," Reinhold, New York, 1950, p. 118.

TABLE 4. *Conductivities.*

10^3C (equiv./l.)	Λ (mho cm.²)	10^5K	10^3C (equiv./l.)	Λ (mho cm.²)	10^5K	10^3C (equiv./l.)	Λ (mho cm.²)	10^5K	10^3C (equiv./l.)	Λ (mho cm.²)	10^5K
(10% Acetone–water)						(25% Acetone–water)					
Acetic acid (7)											
2·231	20·76	1·26	1·054	29·53	1·25	1·916	10·03	0·585	0·5906	17·56	0·581
1·731	23·37	1·25	0·6332	37·64	1·26	1·707	10·62	0·586	0·4240	20·68	0·586
1·489	25·20	1·26	0·2171	59·86	(1·21)	1·430	11·55	0·585	0·3111	23·78	0·584
1·308	26·67	1·25				0·8842	14·49	0·581	0·2336	27·18	0·590
	(Λ_0 = 284·3)						(Λ_0 = 184·7)				
Phenylacetic acid (4)											
2·177	31·04	2·71	1·143	41·86	2·71	2·066	12·43	0·862	0·8289	19·21	0·862
1·684	35·03	2·71	0·6520	52·79	(2·58)	1·768	13·38	0·859	0·7562	20·05	0·862
1·460	37·40	2·71	0·3583	70·43	2·73	1·230	15·88	0·857	0·4633	25·19	0·860
						0·9891	17·67	0·862	0·1806	38·67	0·861
	(Λ_0 = 290·8)						(Λ_0 = 196·5)				
Diphenylacetic acid (1)											
1·264	52·18	4·76	0·5126	77·23	4·76	1·883	14·17	0·958	0·3883	29·79	0·960
1·160	54·18	4·76	0·4187	84·01	4·75	1·732	14·73	0·955	0·3126	32·90	0·961
1·062	56·34	4·75	0·3222	93·60	4·76	1·609	15·29	0·960	0·2028	39·85	0·955
0·7478	65·77	4·76	0·1983	113·1	4·76	0·9195	19·90	0·956			
0·6106	71·79	4·77									
	(Λ_0 = 292·8)						(Λ_0 = 203·5)				
Triphenylacetic acid (2)											
0·05012	(135·6)	—	0·03311	194·4	4·15	0·1991	35·67	0·801	0·1110	46·08	0·799
0·03981	187·7	4·47	0·03121	194·9	4·05	0·1377	42·05	0·803	0·09700	48·86	0·800
	(Assumed Λ_0 = 294·0)					0·1228	44·26	0·806	0·07169	55·53	0·801
							(Assumed Λ_0 = 195·5)				
Trimethylacetic acid (9)											
1·732	14·66	0·589	0·3845	29·94	0·586	1·952	5·336	0·164	0·4474	10·88	0·162
1·230	17·27	0·588	0·2431	36·94	0·583	1·602	5·783	0·159	0·2516	14·29	0·161
0·9215	19·83	0·588	0·2140	39·17	0·583	1·233	6·680	0·164	0·1751	16·02	(0·142)
0·4827	26·95	0·588									
	(Λ_0 = 256·7)						(Λ_0 = 185·3)				
Dineopentylacetic acid (*siccatic acid A*) (11)											
0·1658	40·41	0·385	0·09655	51·15	(0·376)	0·6462	6·377	0·0672	0·4635	7·544	0·0679
0·1233	46·31	0·386	0·08201	55·31	0·381	0·6303	6·423	0·0665	0·3252	8·879	0·0665
0·1185	47·07	0·384	0·07715	56·91	0·382	0·4942	7·201	0·0659	0·2038	11·07	0·0656
	(Assumed Λ_0 = 285·0)					0·4701	7·501	0·0681	0·1291	13·83	0·0659
							(Assumed Λ_0 = 200·0)				
Methylneopentyl-t-butylacetic acid (*siccatic acid B*) (12)											
0·07782	24·84	0·0669	0·06564	27·30	0·0689	0·3262	3·883	0·0146	0·1882	5·227	0·0154
0·06665	26·93	0·0680	0·05749	28·90	0·0680	0·2762	4·288	0·0151	0·07425	9·087	(0·0188)
	(Assumed Λ_0 = 280·0)					0·2277	4·713	0·0151			
							(Assumed Λ_0 = 185·0)				
Propionic acid (8)											
1·972	18·36	1·028	1·030	25·00	1·028	2·106	7·499	0·364	1·041	10·55	0·364
1·633	20·08	1·028	0·7587	28·83	1·025	1·717	8·293	0·365	0·6656	13·00	0·358
1·497	20·95	1·028	0·4390	37·24	1·029	1·675	8·345	0·360	0·4015	16·66	0·364
1·204	23·23	1·029	0·2890	45·04	1·028	1·484	8·880	0·363			
	(Λ_0 = 261·0)						(Λ_0 = 182·5)				

TABLE 4. (*Continued.*)

10^3C (equiv./l.)	Λ (mho cm.²)	10^5K	10^3C (equiv./l.)	Λ (mho cm.²)	10^5K	10^3C (equiv./l.)	Λ (mho cm.²)	10^5K	10^3C (equiv./l.)	Λ (mho cm.²)	10^5K
(10% Acetone–water)						(25% Acetone–water)					
β-Phenylpropionic acid (6)											
2·039	21·76	1·26	0·6273	37·92	1·26	1·863	8·964	0·402	1·032	11·95	0·403
1·789	23·16	1·26	0·3610	48·78	1·26	1·786	9·168	0·403	0·8079	13·44	0·403
1·153	28·54	1·26	0·1965	63·73	1·25	1·544	9·818	0·402	0·4329	18·10	0·402
0·7839	34·20	1·26				1·428	10·21	0·403	0·1894	26·67	0·403
	(Λ_0 = 285·4)						(Λ_0 = 195·7)				
ββ-Diphenylpropionic acid (5)											
1·299	29·27	1·48	0·6196	41·32	1·48	1·656	9·138	0·419	0·4287	17·48	0·420
1·191	30·53	1·48	0·4468	48·11	1·49	1·567	9·395	0·420	0·2960	20·84	0·420
0·8144	36·52	1·49	0·3157	56·02	1·48	1·173	10·80	0·420	0·2173	24·06	0·420
0·7151	38·82	1·49	0·1985	68·39	1·47	0·5053	16·17	0·420	0·1934	25·38	0·420
	(Λ_0 = 286·8)						(Λ_0 = 184·6)				
ββ-Dimethyl-β-phenylpropionic acid (10)											
1·842	14·92	0·537	0·4863	28·19	0·536	1·964	5·295	0·155	0·3897	11·64	0·154
1·502	16·45	0·536	0·4182	30·31	0·537	1·263	6·583	0·155	0·3068	13·06	0·154
1·254	17·99	0·539	0·3146	34·59	0·536.	0·6536	9·057	0·154	0·2148	15·50	0·154
0·6538	24·52	0·537	0·2257	40·21	0·532	0·4929	10·38	0·154			
	(Λ_0 = 281·5)						(Λ_0 = 190·0)				
Benzoic acid (3)											
2·274	34·48	3·52	0·4990	68·23	3·52	2·292	13·28	1·01	0·6575	24·00	1·01
2·006	36·39	3·49	0·4232	73·37	3·54	1·975	14·27	1·01	0·4014	30·20	1·01
1·229	45·64	3·50	0·3366	80·80	3·54	1·630	15·64	1·01	0·2230	39·36	1·01
0·6750	59·75	3·51	0·2028	99·26	3·54	1·243	17·80	1·01	0·1820	42·98	1·01
	(Λ_0 = 291·0)						(Λ_0 = 204·3)				

by Dr. J. T. Young.[9] Other acids were purchased. Solid acids (with two exceptions) were repeatedly recrystallised from conductivity water (di- and tri-substituted acetic and propionic acids, being sparingly soluble, required up to 1 l. for 1 g. of acid). Siccatic acids A and B were recrystallised three times from small amounts of purified acetone, as water proved ineffective. " AnalaR " acetic acid was distilled twice from 2% (w/w) potassium permanganate (about 50% being rejected) and then fractionated. Propionic acid (" purified " quality) was fractionated twice. Trimethylacetic acid was distilled under reduced pressure in an all-glass apparatus.

The final specimens were stored in desiccators over silica gel for at least two weeks, and the m. p.s (Table 1) determined. Equivalent weights of all purified acids were derived by titration with alkali.

Purification of Acetone.—" AnalaR " acetone was fractionated in an all-glass distillation apparatus with a 14 in. column packed with Fenske helices, the heating being by a finely controlled Electrothermal mantle. The middle fraction (about 70%), boiling over a range of not more than 0·2°, was collected. Water contents of the resulting solvent and a few wetted samples (up to 5% of water by weight) were determined by the Karl Fischer technique,[10] and the correlation between water contents and physical properties was in agreement with the relationships given by S. R. C. Hughes: [11] $d_4^{25} = 0{\cdot}7835 + 0{\cdot}0031x$; $\eta_0^{25} = 0{\cdot}00300 + 0{\cdot}00017x$ (where x = % wt. of water). The density of each batch of acetone used for conductivity measurements was determined (100 ml. pyknometer), and the percentage of water calculated by use of the above equations. The mixed solvent (composition accurate to within ±0·01%) was prepared by weight in capped 2 l. conical flasks and allowed to stand for a few hours before use (for very sparingly-soluble acids it was much quicker to dissolve the solid in acetone and then make up by weight with water). The specific conductivities of the 10% and 25% aqueous acetone solutions were 0·5—0·6 gemmho and 0·2—0·3 gemmho respectively, at 25°.

[9] See Dippy and Young, *J.*, 1952, 1817; 1955, 3919.
[10] Mitchell and Smith, " Aquametry," Interscience, New York, 1948.
[11] S. R. C. Hughes, *J.*, 1956, 998.

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Measurement of Conductivities and Calculation of Results.—Conductivities of all solutions were measured as previously described.[12]

Solvent corrections in non-aqueous and partially aqueous solvents are still problematical, since the nature of the impurities must be first established. No solvent correction was applied to aqueous solutions in this work, on the assumption that carbonic acid is the main impurity and its ionisation would be suppressed correspondingly by the addition of organic solvent to water.[13] This was justified by the consistent values of K obtained with " uncorrected " conductivity data.

Λ_0 was evaluated by Ives's extrapolation method [14] by use of appropriate physical constants for the solvents, as shown in Table 3; individual values of K were then calculated as usual. For triphenylacetic acid and siccatic acids (A and B), Λ_0 values were assumed, since the low solubility of these acids did not permit the use of extrapolation. The success of the extrapolation as applied to partially aqueous solvents is shown by (i) the constancy in the values of K over the range where the limiting Debye–Hückel law applies, (ii) the satisfactory correlation of K values in different solvents, as shown in Fig. 1, and (iii) the fluctuations in Λ_0 for different acids in each solvent which show the expected change of about ± 10 units about a mean value (although the plot of $\Lambda_0\eta$ against η reveals a regular decrease indicating, presumably, change in the mode of solvation of the ions).

One of us (A. R.) thanks the Governing Body of the Chelsea College of Science and Technology for a Research Assistantship.

CHEMISTRY DEPARTMENT, CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY,
LONDON, S.W.3. [*Received, September 26th*, 1958.]

[12] Dippy, S. R. C. Hughes, and Laxton, *J.*, 1954, 1470.
[13] Speakman, *Trans. Faraday Soc.*, 1954, **50**, 236.
[14] Ives, *J.*, 1933, 731; 1943, 511.

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282. *The Structure of Tazettine. A Synthesis of the Emde Degradation Product derived from Tazettamide.*

By HIROSHI IRIE, YOSHISUKE TSUDA, and SHOJIRO UYEO.

The compound (VI; R = OMe, R′ = H) has been synthesised by a stereospecific route. Its identity with the Emde degradation product of an amine derived from tazettamide has provided further confirmation of the detailed structure of tazettine.

WE have shown earlier [1] that tazettine, an alkaloid occurring in many plants of the *Amaryllidaceae*, can best be represented by the formula (I; R = OMe, R′ = H, R″ = Me, R‴ = OH). The degradative sequence leading to (VI; R = OMe, R′ = H) (see Chart 1) started from tazettamide (II; R = OMe, R′ = H, R″ = Me), a product of the manganese dioxide oxidation of tazettine.[2]

We have recently found that two further compounds are formed during the initial oxidation. One of them is 6-*p*-hydroxyphenylpiperonaldehyde, as shown by synthesis, and the other is *N*-demethyltazettamide (II; R = OMe, R′ = R″ = H), identical with the product obtained by manganese dioxide oxidation of nortazettine (I; R = OMe, R′ = R″ = H, R‴ = OH) which in turn was prepared by alkaline rearrangement [3] of hæmanthidine.[4] Such an elimination of a methyl group attached to nitrogen has also been demonstrated by Henbest and Thomas.[5]

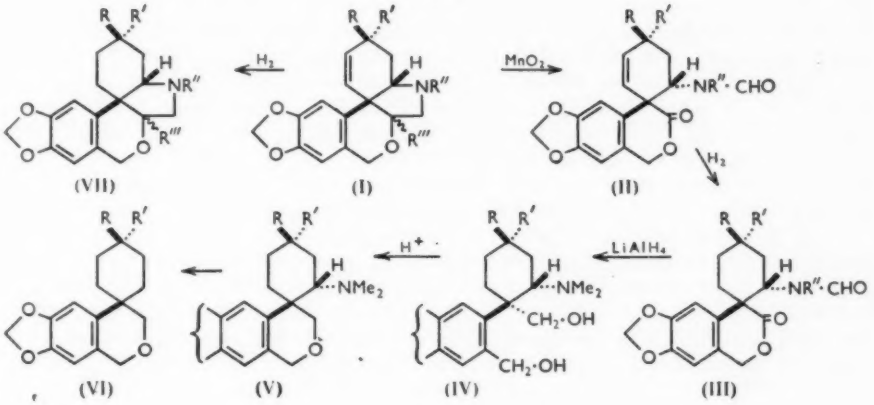
We have further noted that when tazettamide was reduced catalytically over palladium–charcoal, demethoxydihydrotazettamide (III; R = R′ = H, R″ = Me) was produced

[1] Ikeda, Taylor, Tsuda, Uyeo, and Yajima, *J.*, 1956, 4749.
[2] Highet and Wildman, *Chem. and Ind.*, 1955, 1159.
[3] Fales, Highet, Uyeo, and Wildman, unpublished observation.
[4] Uyeo, Fales, Highet, and Wildman, *J. Amer. Chem. Soc.*, 1958, **80**, 2590.
[5] Henbest and Thomas, *J.*, 1957, 3032.

XUM

as a by-product which can be satisfactorily separated from the major product, dihydrotazettamide (III; R = OMe, R′ = H, R″ = Me), only by chromatography. Re-examination of the hydrogenation products of tazettine and deoxytazettine (I; R = OMe, R′ = R‴ = H, R″ = Me) has afforded similar results, *viz.*, that demethoxydihydrotazettine (VII; R = R′ = H, R″ = Me, R‴ = OH) and demethoxydeoxydihydrotazettine (VII; R = R′ = R‴ = H, R″ = Me), respectively, were invariably accompanied by dihydrotazettine (VII; R = OMe, R′ = H, R″ = Me, R‴ = OH) and deoxydihydrotazettine (VII; R = OMe, R′ = R‴ = H, R″ = Me), respectively.

Chart I.



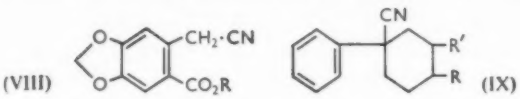
An allylic acetoxyl group was found to be eliminated even more readily by hydrogenation. Thus diacetyltazettinol (I; R = R‴ = OAc, R′ = H, R″ = Me) or diacetyl-*iso*tazettinol (I; R = H, R′ = R‴ = OAc, R″ = Me) over palladium–charcoal in acidic solution gave the same products, acetyldemethoxytazettine (I; R = R′ = H, R″ = Me, R‴ = OAc) and demethoxydihydrotazettine (VII; R = R′ = H, R″ = Me, R‴ = OH), but monoacetyl*iso*tazettinol (I; R = H, R′ = OAc, R″ = Me, R‴ = OH) was converted into demethoxytazettine (I; R = R′ = H, R″ = Me, R‴ = OH), subsequent hydrogenation of which over platinic oxide furnished its dihydro-derivative (VII; R = R′ = H, R″ = Me, R‴ = OH). Hydrogenolysis also occurred with platinic oxide since diacetyl-*iso*tazettinol afforded dihydro*iso*tazettinol, demethoxydihydrotazettine, and demethoxydeoxydihydrotazettine (VII; R = R′ = R‴ = H, R″ = Me). Because of the above type of side reaction, the Emde product (VI; R = OMe, R′ = H) derived from dihydrotazettamide was sometimes contaminated by its demethoxylated derivative (VI; R = R′ = H), unless chromatographically purified dihydrotazettamide was used as a starting material.

For the synthesis of compounds related to (VI), the most logical starting material seemed to be the ester (VIII; R = Me) which was readily obtained from the known acid [6] (VIII; R = H). Attempts to condense the ester with methyl β-bromopropionate or β-bromopropionitrile in the presence of sodium amide or sodium hydride in a variety of solvents under various conditions were fruitless. The model compound, benzyl cyanide, on the other hand, readily condensed in good yields with the above reagents in toluene in the presence of excess of sodium amide to afford in one step the compounds (IX; R = NH, R′ = CN; and R = O, R′ = CO_2Me, respectively), both of which were convertible into 4-cyano-4-phenyl*cyclo*hexanone (IX; R = O, R′ = H) by strong acid.

[6] Edwards, *J.*, 1926, 813.

Michael condensation of the ester (VIII; R = Me) with acrylonitrile or methyl acrylate also failed and hence the use of this compound as the starting material was abandoned.

Next, we tried unsuccessfully to condense 3 : 4-methylenedioxybenzyl cyanide (X) with β-bromopropionitrile or methyl β-bromopropionate in the presence of sodium amide



(VIII) (IX)

or sodium hydride. On the other hand, the compound (X) reacted readily with acrylonitrile or methyl acrylate in the presence of alkaline reagents such as sodium methoxide or Triton B, yielding γ-cyano-γ-(3 : 4-methylenedioxyphenyl)pimelonitrile (XI) or the analogous dimethyl ester (XII; R = Me). The best yield of the latter (XII; R = Me) was obtained by the use of Triton B in boiling *tert.*-butyl alcohol. Hydrolysis of the trinitrile (XI) in concentrated hydrochloric acid furnished an acid shown to be an imidocarboxylic acid (XIII; R = H) from the infrared spectrum and its non-identity with the acid (XII; R = H) obtained by saponification of the ester (XII; R = Me). This was not surprising since Campbell [7] observed that γ-cyano-γ-phenylpimelonitrile was smoothly converted into α-2-carboxyethyl-α-phenylglutarimide by treatment with sulphuric acid and Mariella, Clutter, and Ebner [8] showed that γ-cyano-γ-ethoxycarbonylpimelonitrile and γγ-dicyanopimelonitrile, among other compounds, gave with concentrated hydrochloric acid α-ethoxycarbonyl-α-2-carboxyethylglutarimide and 2 : 8-diaza*spiro*-[5 : 5]hendecane-1 : 3 : 7 : 9-tetraone [3 : 3′-*spiro*bi(piperidine-2 : 6-dione)], respectively. The acid (XIII; R = H) gave with diazomethane an *N*-methyl ester (XIII; R = Me), as proved by analysis and by the absence of NH absorption in the 3 μ region. The ester (XIII; R = Me) thus formed was converted into an amido-ketone (XIV; R = H), albeit in a low yield, by treatment with sodium methoxide followed by strong acid, as a result of methanolysis of the imide linkage to an amide diester followed by cyclisation under Dieckmann conditions and decarboxylation of the resulting β-keto-ester (XIV; R = CO_2Me). An attempt to convert the acid (XIII; R = H) into the ketone (XV; R = H) under the Blanc conditions by first refluxing it with acetic anhydride and then heating it at 200° under reduced pressure gave only a minute amount of the desired product which showed correct analytical values and infrared absorption bands at 2252 (CN) and 1724 cm.$^{-1}$ (CO).

The same ketone (XV; R = H) was made in far better yield by Dieckmann cyclisation of the diester (XII; R = Me) followed by decarboxylation in a strong acid. Formation of a diethyl ketal (XVIII; R = Et) of the ketone as a by-product was sometimes observed when ethanol was used as a solvent.

The trinitrile (XI) underwent a Ziegler cyclisation in good yield, but in a preliminary experiment difficulties were encountered in saponifying and decarboxylating the product (XVI) to the ketone (XV; R = H) and hence this compound was not further investigated. The cyano-ketone (XV; R = H) was reduced with sodium borohydride in methanol to 4-cyano-4-(3 : 4-methylenedioxyphenyl)*cyclo*hexanol (XVII). The experimental conditions used were such that we were able to isolate only one of the possible isomers: the bulkiness of the aryl group probably determines the preferred conformation and, since the reduction method would be expected to yield an equatorial hydroxyl group, this would be expected to be in *trans*-position to the aryl residue, as shown in (XVII). The reduction gave the dimethyl ketal (XVIII; R = Me) as by-product: no other analogous case is known to us. This ketal exhibited no absorption in the 3 μ region but there was a strong absorption at about 1100 cm.$^{-1}$ and further it regenerated the parent ketone when heated with acid.

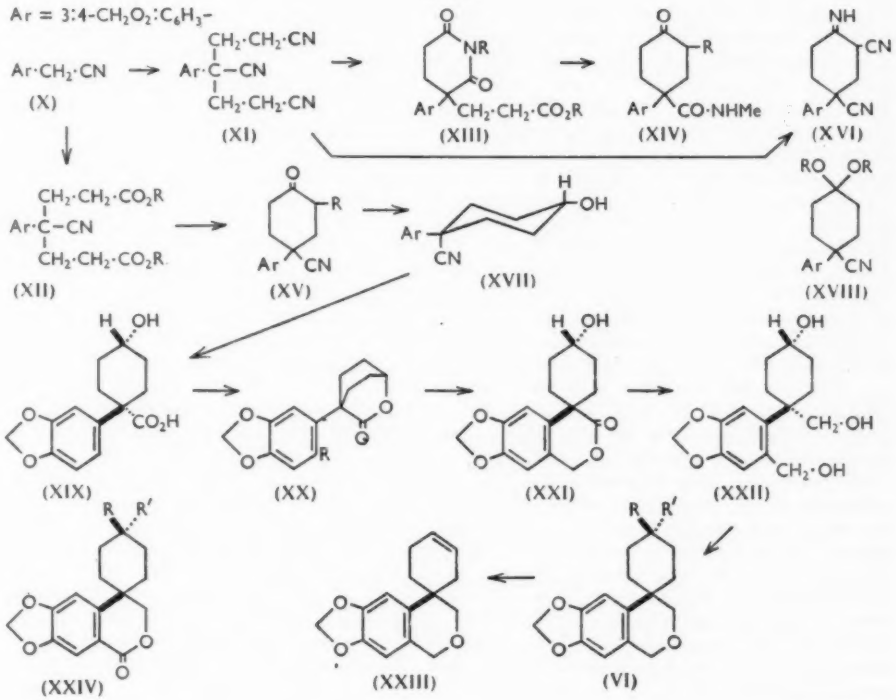
The hydroxy-nitrile (XVII) was then hydrolysed with potassium hydroxide in boiling

[7] Campbell, *J.*, 1954, 1377; cf. Hey and Nagdy, *J.*, 1954, 1204; Blair and Hey, *J.*, 1957, 2921.
[8] Mariella, Clutter, and Ebner, *J. Org. Chem.*, 1955, **20**, 1702.

diethylene glycol, to give the hydroxy-acid (XIX) which with acetic anhydride, in agreement with the stereochemical assignment, passed into the lactone (XX; R = H) (>C=O band at 1739 cm.$^{-1}$). The hydroxy-acid was regenerated on alkaline hydrolysis of the lactone.

A methylene group was then introduced into the position 6 of the aryl nucleus by heating the hydroxy-acid (XIX) or the lactone (XX; R = H) with paraformaldehyde in

Chart 2.



concentrated hydrochloric acid, a chloromethyl compound (XX; R = CH_2Cl) being formed. Alkaline hydrolysis of this, followed by relactonisation, afforded a compound, $C_{15}H_{16}O_5$, for which two alternative structures (XXI) or (XX; R = CH_2OH) were possible: the energetically more stable (XXI) was preferred and in agreement the lactone band at 1724 cm.$^{-1}$ was at a slightly longer wavelength than for the lactones described above. The hydroxy-lactone (XXI) was reduced with lithium aluminium hydride to a triol (XXII) which readily underwent acid-catalysed cyclisation to the hydroxy-ether (VI; R = H, R′ = OH).

If our ideas concerning the structure of tazettine were correct, the same compound was theoretically derivable from *iso*tazettinol by the degradative sequence sketched in Chart 1. Hydrogenation of *iso*tazettinol (I; R = H, R′ = R‴ = OH, R″ = Me) gave dihydro-*iso*tazettinol (VII; R = H, R′ = R‴ = OH, R″ = Me) which was oxidised with manganese dioxide to give an amide-lactone (III; R = H, R′ = OH, R″ = Me). This was converted smoothly into the ether (VI; R = H, R′ = OH) in a manner similar to that employed for the analogous compound (III; R = OMe, R′ = H, R″ = Me). The product thus obtained was, as expected, optically inactive and identical with the synthetic compound.

The synthetic compound (VI; R = H, R′ = OH) was converted into the degradation

product of tazettine by way of the *O*-toluene-*p*-sulphonate which underwent S_N2 replacement with methoxide ion, the expected olefinic by-product (XXIII) being also formed.

Experimental

Ultraviolet absorption spectra were determined for 95% ethanol solutions, and infrared spectra were taken on Nujol mulls unless otherwise stated.

Isolation of Hippeastrine and Hæmanthidine from Lycoris radiata.—The mother-liquor (33 g.) of an extract of *Lycoris radiata* from which most of the lycorine, lycorenine, homolycorine, tazettine, lycoramine, galanthamine, and phenolic alkaloids had been separated, was dissolved in 5% hydrochloric acid (1 l.), washed with chloroform, brought to pH 7·2 with potassium carbonate, and extracted with ethyl acetate (1·5 l.). The dried extract was evaporated to dryness and the residue (7 g.) crystallised from ethanol to give tazettine (2 g.). The mother-liquor from the crystallisation of tazettine was chromatographed in benzene over alumina (50 g.), yielding the following fractions: (i) Benzene eluate (500 ml.), an oil (2 g.). (ii) Ethyl acetate–benzene eluate (1 : 19, 500 ml.; and 1 : 9, 500 ml.), tazettine (0·8 g.). (iii) Ethyl acetate–benzene (1 : 1) eluate (1 l.), hippeastrine [9] (1 g.), prisms (from acetone), m. p. 214—215°, $[\alpha]_D$ +147° (*c* 0·9 in EtOH) {lit.,[10] m. p. 214—215°, $[\alpha]_D$ +160° (in $CHCl_3$)}, $\lambda_{max.}$ 227, 268, and 308 mμ (log ε 4·51, 3·86, and 3·89) (Found: C, 64·6; H, 5·4; N, 4·4. Calc. for $C_{17}H_{17}O_5N$: C, 64·8; H, 5·4; N, 4·4%); a mixed m. p. and comparison of the infrared spectra completed the identification of this alkaloid. (iv) A fraction eluted with ethyl acetate (1·5 l.) was taken up into chloroform; a small portion (20 mg.) remained undissolved. The solution was evaporated to dryness and the residue crystallised from ethyl acetate to furnish hæmanthidine (0·2 g.), m. p. 187—189°, $[\alpha]_D$ −43° (*c* 0·88 in $CHCl_3$) {lit.,[11] m. p. 189—190°, $[\alpha]_D$ −41° (in $CHCl_3$)}, $\lambda_{max.}$ 241 and 293 mμ (log ε 3·46 and 3·62) (Found: C, 63·8; H, 5·9; N, 4·4. Calc. for $C_{17}H_{19}O_5N$: C, 64·3; H, 6·0; N, 4·4%); the m. p. was undepressed on admixture with the authentic alkaloid and the infrared spectrum was identical with that of hæmanthidine; the picrate formed yellow needles, m. p. 207—208° (decomp.) [lit.,[11] m. p. 208° (decomp.)].

Nortazettamide from Hæmanthidine.—Hæmanthidine (0·16 g.) in 10% methanolic sodium methoxide (5 ml.) was heated under reflux for 40 min. The methanol was evaporated, and the residue in water (20 ml.) was extracted with chloroform after saturation with ammonium chloride. The chloroform extract afforded nortazettine (0·15 g.) as a gum which was characterised as its hydrochloride, needles, m. p. 198—200° (lit.,[3] m. p. 197—201°) (from ethanol–acetone). Nortazettine (90 mg.) in chloroform (12 ml.) was stirred with manganese dioxide (1 g.) at room temperature for 15 hr. The manganese dioxide was filtered off and washed with chloroform and the combined filtrate and washings were shaken with 5% hydrochloric acid and water and concentrated to dryness. Crystallisation of the residue from ethanol gave nortazettamide (II; R = OMe, R′ = R″ = H) (50 mg.) as prisms, m. p. 180—181° from ethanol.

Manganese Dioxide Oxidation of Tazettine.—Tazettine (1·3 g.) was oxidised with manganese dioxide and worked up as described previously,[1] to afford a crude product which was chromatographed in benzene over alumina (10 g.). Tazettamide (0·45 g.) was eluted with benzene (50 ml.) and crystallised from ethanol, then having m. p. 174°. Further elution with the same solvent (450 ml.) furnished *nortazettamide* (0·15 g.), prisms (from ethanol), m. p. 179—181°, $[\alpha]_D$ +250° (*c* 1·0 in EtOH), $\lambda_{max.}$ 245 and 290 mμ (log ε 3·66 and 3·76), $\nu_{max.}$ 3125 (NH), 1748 (lactone), 1661 and 1618 (amide), and 1555 $cm.^{-1}$ (NH) in Nujol mull and 3413 (NH), 1732 (lactone), and 1687 $cm.^{-1}$ (amide) in chloroform (Found: C, 61·7; H, 5·2; N, 4·3; OMe, 9·4. $C_{17}H_{17}O_6N$ requires C, 61·6; H, 5·2; N, 4·2; OMe, 9·4%). The m. p. was not depressed on admixture with a sample derived from nortazettine. Further elution with benzene (1 l.) gave 6-p-*hydroxyphenylpiperonaldehyde* (55 mg.), plates, m. p. 170—172° (from dilute ethanol), $\lambda_{max.}$ 245, 270, and 330 mμ (log ε 4·31, 4·17, and 3·79), $\nu_{max.}$ 3225—3125 (OH), 1653 (CO), and 1616 $cm.^{-1}$ (benzene) (Found: C, 69·4; H, 4·1. $C_{14}H_{10}O_4$ requires C, 69·4; H, 4·2%).

The aldehyde, with acetic anhydride in pyridine, gave an *acetate*, needles, m. p. 164—165° after crystallisation from dilute ethanol (Found: C, 67·0; H, 4·3. $C_{16}H_{12}O_5$ requires C, 67·6;

[9] We are indebted to Dr. W. C. Wildman, National Institutes of Health, Maryland, U.S.A., for authentic samples of hippeastrine and hæmanthidine.
[10] Boit, *Chem. Ber.*, 1956, **89**, 1129.
[11] *Idem, ibid.*, 1954, **87**, 1339.

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H, 4·3%), and afforded on reduction with sodium borohydride in methanol 2-*p*-hydroxyphenyl-4 : 5-methylenedioxybenzyl alcohol, m. p. and mixed m. p. 186—188°.[1]

Hydrogenation of Tazettine.—Tazettine (1·65 g.) in ethanol (15 ml.) and acetic acid (7 ml.) was hydrogenated in the presence of platinum oxide (0·4 g.). After 5 hr. the solution was filtered, evaporated and extracted with ether after basification with aqueous ammonia. The ethereal extract was concentrated and the residue crystallised from ether to give dihydrotazettine[12] (0·97 g.), prisms, m. p. and mixed m. p. 165—167°. Evaporation of the mother-liquor and chromatography in benzene over alumina gave *demethoxydihydrotazettine* (VII; R = R′ = H, R″ = Me, R‴ = OH) (0·19 g.), prisms, m. p. 168—169° (from ether), $[\alpha]_D$ +22·4° (*c* 0·3 in $CHCl_3$) (Found: C, 67·5; H, 7·1; OMe, 0. $C_{17}H_{21}O_4N$ requires C, 67·3; H, 7·0%). The *picrate* formed needles, m. p. 200—202° (decomp.), from ethanol (Found: C, 51·6; H, 4·3. $C_{17}H_{21}O_4N,C_6H_3O_7N_3$ requires C, 51·9; H, 4·4%). Further elution with chloroform afforded an additional crop (0·1 g.) of dihydrotazettine.

Hydrogenation of Deoxytazettine.—Deoxytazettine (I; R = OMe, R′ = R‴ = H, R″ = Me) (0·5 g.) in ethanol (10 ml.) and acetic acid (5 ml.) was hydrogenated for 5 hr. The crude product was converted into a mixture of picrates which was separated in acetone into a slightly soluble and a more soluble compound. The less soluble one was crystallised from acetone, to yield *demethoxydeoxydihydrotazettine picrate* (VII; R = R′ = R‴ = H, R″ = Me) (70 mg.), yellow needles, m. p. 225—227° (decomp.) (Found: C, 53·5; H, 4·7; N, 11·1; OMe, 0. $C_{17}H_{21}O_3N,C_6H_3O_7N_3$ requires C, 53·5; H, 4·7; N, 10·9%). The free base regenerated from the picrate by filtration in chloroform through a column of alumina was an oil, $[\alpha]_D$ +46° (*c* 3·55 in EtOH), whose *methiodide* crystallised from ethanol as prisms, m. p. 294° (decomp.) (Found: C, 49·8; H, 5·6; N, 3·4. $C_{17}H_{21}O_3N,CH_3I$ requires C, 50·4; H, 5·6; N, 3·2%). The more soluble picrate was crystallised from ethanol, affording deoxydihydrotazettine picrate[1] (VII; R = OMe, R′ = R‴ = H, R″ = Me) (0·15 g.), m. p. and mixed m. p. 190—191° (decomp.).

Hydrogenation of Tazettamide.—Tazettamide[1] (0·3 g.) in ethanol (20 ml.) was hydrogenated over 10% palladium–carbon (0·25 g.) at room temperature for 15 hr. After removal of the catalyst and concentration to dryness, the residue (0·285 g.) was crystallised four times from ethanol, to furnish dihydrotazettamide[1,2] (20 mg.), m. p. and mixed m. p. 156—157°. The mother-liquors were evaporated to dryness and chromatographed in benzene over acid-washed alumina. A benzene eluate gave an additional quantity of dihydrotazettamide (0·15 g.). Elution with benzene–chloroform (1 : 1) afforded a mixture, m. p. 148—152, and further elution with chloroform yielded *demethoxydihydrotazettamide* (III; R = R′ = H, R″ = Me) (10 mg.), needles, m. p. 213—215° (from ethanol), $\nu_{max.}$ 1715 (lactone), and 1661 cm.$^{-1}$ (amide) (Found: C, 62·8; H, 6·0; OMe, 0. $C_{17}H_{19}O_5N,\frac{1}{2}H_2O$ requires C, 62·6; H, 6·2%). The combined mother-liquors and intermediate fractions were rechromatographed as above and additional quantities of dihydrotazettamide (65 mg.) and demethoxydihydrotazettamide (12 mg.) were isolated. Demethoxydihydrotazettamide was also obtained by the hydrogenation of *demethoxytazettamide* (II; R = R′ = H, R″ = Me), prisms, m. p. 205—206° (from ethanol, $\nu_{max.}$ 1731 (lactone) and 1667 cm.$^{-1}$ (amide) in chloroform (Found: C, 64·4; H, 5·5. $C_{17}H_{17}O_5N$ requires C, 64·8; H, 5·4%), which in turn was prepared by the manganese dioxide oxidation of demethoxytazettine (see below).

Hydrogenation of Nortazettamide.—Nortazettamide (0·15 g.) was hydrogenated in ethanol (20 ml.) over 10% palladium–carbon (0·15 g.) for 8 hr. Chromatography of the crude product in benzene over acid-washed alumina gave *demethoxydihydronortazettamide* (III; R = R′ = R″ = H) (85 mg.), prisms, m. p. 190—191° (from benzene), $[\alpha]_D$ −104·7° (*c* 0·6 in EtOH), $\nu_{max.}$ 3289 (NH), 1733 (lactone), 1681, and 1661 cm.$^{-1}$ (amide) (Found: C, 63·2; H, 5·5; OMe, 0. $C_{16}H_{17}O_5N$ requires C, 63·4; H, 5·7%).

Hydrogenation of Di-O-acetyltazettinol.—Diacetyltazettinol (I; R = R‴ = OAc, R′ = H, R″ = Me) (0·11 g.) in 2% hydrochloric acid (20 ml.) was hydrogenated in the presence of 15% palladium–carbon (0·1 g.) for 7 hr. The resulting crude product was chromatographed in benzene over alumina. The benzene eluate gave O-*acetyldemethoxytazettine* (I; R = R′ = H, R″ = Me, R‴ = OAc) (30 mg.), needles, m. p. 170—171° from light petroleum (b. p. 60—80°), $\nu_{max.}$ 1742 cm.$^{-1}$ (acetyl) (Found: C, 66·7; H, 6·1. $C_{19}H_{21}O_5N$ requires C, 66·5; H, 6·2%). Further elution with chloroform gave demethoxydihydrotazettine (VII; R = R′ = H, R″ = Me, R‴ = OH) (60 mg.), prisms, m. p. and mixed m. p. 167—168° (from ether).

[12] Kondo, Ikeda, and Taga, *Ann. Report ITSUU Lab.*, 1954, **5**, 72.

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Hydrogenation of Diacetyl-iso-tazettinol.—(*a*) Di-*O*-acetyl-*iso*tazettinol (I; R = H, R′ = R‴ = OAc, R″ = Me) (0·13 g.) in 1% hydrochloric acid (20 ml.) was hydrogenated over 15% palladium–carbon (0·1 g.) for 7 hr. After working up as above, *O*-acetyldemethoxytazettine (30 mg.) and demethoxydihydrotazettine (75 mg.) were isolated.

(*b*) Diacetyl-*iso*tazettinol (0·2 g.) in ethanol (5 ml.) and acetic acid (5 ml.) was hydrogenated over platinum oxide (0·11 g.) for 7 hr. The crude product was chromatographed in benzene over alumina, and the benzene eluate gave demethoxydeoxydihydrotazettine (VII; R = R′ = R‴ = H, R″ = Me) as its picrate (20 mg.), m. p. and mixed m. p. 225—227° (decomp.). Benzene–chloroform (1 : 1) and chloroform eluates were combined and rechromatographed. Elution with chloroform then gave demethoxydihydrotazettine (20 mg.), m. p. and mixed m. p. 162—165°. Chloroform–acetone and acetone eluates from the second column were combined and rechromatographed to furnish dihydro-*iso*tazettinol (see below) (5 mg.), m. p. and mixed m. p. 246—248°.

Mono-O-acetyl-iso-tazettinol (I; R = H, R′ = OAc, R″ = Me, R‴ = OH).—*iso*Tazettinol (I; R = H, R′ = R‴ = OH, R″ = Me) (80 mg.) in pyridine (2 ml.) and acetic anhydride (1 ml.) was kept at 10° overnight. After addition of water (10 ml.) and sodium carbonate, the mixture was extracted with ether, and the ether dried and evaporated to give a gum which crystallised from benzene to give *mono-O-acetyl-iso-tazettinol*, plates, m. p. 193—194°, $[\alpha]_D$ +308° (*c* 0·6 in $CHCl_3$), $\nu_{max.}$ 3436 (OH) and 1712 cm.$^{-1}$ (acetyl) (Found: C, 63·7; H, 5·8. $C_{19}H_{21}O_8N$ requires C, 63·5; H, 5·9%). Chromatography of the mother-liquors gave from the benzene eluate diacetyl-*iso*tazettinol (20 mg.), m. p. and mixed m. p. 148—150°, and an additional crop of monoacetyl-*iso*tazettinol from the chloroform eluate (total yield, 50 mg.). Monoacetyl-*iso*-tazettinol regenerated *iso*tazettinol on hydrolysis in 3% methanolic potassium hydroxide.

Hydrogenation of Monoacetyl-iso-tazettinol.—Monoacetyl-*iso*tazettinol (65 mg.) in ethanol (3 ml.) and 1% hydrochloric acid (20 ml.) was hydrogenated over 5% palladium–carbon (0·1 g.) for 3 hr. The catalyst was removed and the filtrate made alkaline with aqueous ammonia and extracted with ether, which was dried and evaporated, to yield *demethoxytazettine* (I; R = R′ = H, R″ = Me, R‴ = OH) (50 mg.) as needles, m. p. 193—194° (from ethanol), depressed to 160—170° on admixture with the starting material (Found: C, 67·7; H, 6·5. $C_{17}H_{19}O_4N$ requires C, 67·8; H, 6·4%). The picrate crystallised from ethanol as yellow needles, m. p. 200°. The acetate (I; R = R′ = H, R″ = Me, R‴ = OAc) was prepared by use of sodium acetate in acetic anhydride on a water-bath for 2 hr. It formed needles from light petroleum (b. p. 60—80°) and had m. p. and mixed m. p. 170—171°.

Hydrogenation of Demethoxytazettine.—Demethoxytazettine (40 mg.) in ethanol (8 ml.) was hydrogenated over platinum oxide (40 mg.) for 6 hr., to furnish demethoxydihydrotazettine (VII; R = R′ = H, R″ = Me, R‴ = OH), prisms (from ether), m. p. and mixed m. p. 167—168°.

Demethoxydeoxydihydrotazettine (VII; R = R′ = R‴ = H, R″ = Me).—Demethoxydihydrotazettine (40 mg.) obtained as above was reduced in refluxing tetrahydrofuran with excess of lithium aluminium hydride in 3 hr. The crude diol was heated in 5% sulphuric acid (20 ml.) for 2 hr. on a water-bath. Basification followed by extraction with ether gave an oil (VII; R = R′ = R‴ = H, R″ = Me) characterised as its picrate, needles, m. p. and mixed m. p. 225—227° (decomp.) from acetone.

Demethoxydeoxytazettine (I; R = R′ = R‴ = H, R″ = Me).—Demethoxytazettine (30 mg.) was treated with lithium aluminium hydride, and the resulting diol dehydrated with sulphuric acid in the way similar to that described above. Demethoxydeoxytazettine was isolated as its *picrate*, yellow needles, m. p. 242—244° (decomp.) (from ethanol) (Found: C, 53·6; H, 4·2; N, 10·6. $C_{17}H_{19}O_3N,C_6H_3O_7N_3$ requires C, 53·7; H, 4·3; N, 10·9%).

Dihydro-iso-tazettinol (VII; R = H, R′ = R‴ = OH, R″ = Me).—*iso*Tazettinol (0·55 g.) in ethanol (40 ml.) and acetic acid (2 ml.) was hydrogenated over platinum oxide (0·15 g.) for 2·5 hr. After working up, *dihydro-iso-tazettinol* (0·5 g.) was isolated as prisms, m. p. 250° (from ethanol) (Found: C, 64·5; H, 6·5; N, 4·6. $C_{17}H_{21}O_5N$ requires C, 63·9; H, 6·6; N, 4·4%). The hydrochloride, needles from ethanol–ether, had m. p. 186° (decomp.).

Deoxydihydro-iso-tazettinol (VII; R = R‴ = H, R′ = OH, R″ = Me).—(*a*) Dihydro-*iso*-tazettinol (0·1 g.) was refluxed for 5 hr. in tetrahydrofuran (5 ml.) with excess of lithium aluminium hydride. The resulting triol was heated in 5% sulphuric acid (20 ml.) on the water-bath for 2 hr. The acidic solution was basified with aqueous ammonia and extracted with ether to give an oil (63 mg.) whose *picrate* had m. p. 198° (from ethanol) (Found: C, 52·2; H, 4·5. $C_{17}H_{21}O_4N,C_6H_3O_7N_3$ requires C, 51·9; H, 4·4%). The picrate in acetone–chloroform

was filtered through a column of alumina, yielding the free *base* as prisms, m. p. 155° (from ether–light petroleum; b. p. 60—80°) (Found: C, 67·2; H, 6·8. $C_{17}H_{21}O_4N$ requires C, 67·3; H, 7·0%). (*b*) Deoxy*iso*tazettinol [1] (I; R = R‴ = H, R′ = OH, R″ = Me) (50 mg.) in ethanol (10 ml.) was hydrogenated over platinum oxide (50 mg.) for 4 hr. The catalyst was removed and the filtrate concentrated to dryness, to furnish deoxydihydro*iso*tazettinol, characterised as its picrate, m. p. 198°.

Reduction of Dihydrotazettamide.—The treatment of dihydrotazettamide with lithium aluminium hydride and subsequent cyclisation of the resulting diol (IV; R = OMe, R′ = H) were re-investigated. Starting with chromatographically purified dihydrotazettamide, the amino-ether (V; R = OMe, R′ = H) was obtained as an oil which was converted into its picrate. This formed yellow needles, m. p. 238—240° (decomp.) [lit.,[1] m. p. 226—228° (decomp.)], on crystallisation from acetone and then methanol.

Emde Degradation of the Amino-ether (V; R = OMe, R′ = H).—This reaction was also reinvestigated with a sample of the amino-ether regenerated from its picrate obtained as above. The *methiodide* of the amino-ether crystallised as deliquescent needles, m. p. 220—221°, $[\alpha]_D$ −50° (*c* 0·4 in MeOH), from methanol–ether (Found: C, 48·5; H, 6·1. $C_{18}H_{28}O_4N,CH_3I,\frac{1}{2}H_2O$ requires C, 48·5; H, 6·2%). The methiodide (0·37 g.) was subjected to the Emde degradation under the conditions described in the previous paper.[1] The resulting oil (0·18 g.) was passed in benzene through a column of alumina, concentrated, and kept in a refrigerator, to give the ether (VI; R = OMe, R′ = H) as prisms, m. p. 49—53°. On seeding with a synthetic sample of (VI; R = OMe, R′ = H) (m. p. 89—90°) (see below), this material crystallised from ethanol as prisms, m. p. and mixed m. p. 89—90° (Found: C, 69·9; H, 7·3. Calc. for $C_{16}H_{20}O_4$: C, 69·5; H, 7·3%). The infrared spectrum was identical with that of the synthetic compound.

When a sample (1·5 g.) of dihydrotazettamide, which had been obtained by one crystallisation of the hydrogenation product of tazettamide, was treated as above and the resulting Emde product crystallised repeatedly from ethanol, the product (VI; R = OMe, R′ = H) (0·5 g.) was isolated as the high-melting form, m. p. and mixed m. p. 89—90°. The mother-liquors (0·2 g.) from the crystallisation were chromatographed in benzene over alumina (30 g.). The first benzene eluate gave leaflets, m. p. 60—62°, and the following benzene eluate gave prisms, (50 mg.), m. p. 89—90°, identical with (VI; R = OMe, R′ = H). The former fraction was rechromatographed in benzene over alumina (50 g.) and 6 : 7-*methylenedioxy*iso*chroman*-4-spirocyclo*hexane* (VI; R = R′ = H) (35 mg.) was isolated from the first benzene eluate. It crystallised from ethanol as prisms, m. p. 56—57°, undepressed on admixture with the synthetic sample (Found: C, 72·7; H, 7·3; OMe, 0. $C_{15}H_{18}O_3$ requires C, 73·1; H, 7·4%). Further elution with benzene gave an additional crop (70 mg.) of (VI; R = OMe, R′ = H).

3 : 4-*Dihydro*-4′-*methoxy*-6 : 7-*methylenedioxy*iso*coumarin*-4-spiro-1′-cyclo*hexane* (XXIV; R = OMe, R′ = H).—Potassium permanganate (0·15 g.) in acetone (10 ml.) was added dropwise with stirring to 4′-methoxy-6 : 7-methylenedioxy*iso*chroman-4-*spiro*-1′-*cyclo*hexane (VI; R = OMe, R′ = H) (50 mg.) in acetone (20 ml.) at 15° during 8 hr. After a further 12 hours' stirring, sulphur dioxide was bubbled into the mixture which was then acidified with 1% sulphuric acid (30 ml.) and extracted with ether. The extract furnished the *lactone* (XXIV; R = OMe, R = H), m. p. 144—146°, prisms (from ether), $\lambda_{max.}$ 226, 267, and 306 mμ (log ε 4·32, 3·73, and 3·76), $\nu_{max.}$ 1715 (lactone), and 1613 cm.$^{-1}$ (benzene) in KBr (Found: C, 66·0; H, 6·2. $C_{16}H_{18}O_5$ requires C, 66·2; H, 6·3%).

3 : 4-*Dihydro*-6 : 7-*methylenedioxy*iso*coumarin*-4-spirocyclo*hexane* (XXIV; R = R′ = H).—6 : 7-Methylenedioxy*iso*chroman-4-*spirocyclo*hexane (20 mg.) and potassium permanganate (0·1 g.) were stirred in acetone (25 ml.) at 15° for 20 hr. A saturated solution of sulphur dioxide and dilute sulphuric acid were added to the mixture which was then extracted with ether. Evaporation of the ether gave a residue which was filtered in benzene through a column of alumina and crystallised from light petroleum (b. p. 60—80°), to afford the *lactone* (XXIV; R = R′ = H) as leaflets, m. p. 125—126°, $\lambda_{max.}$ 226, 267, and 307 mμ (log ε 4·33, 3·75, and 3·79) (Found: C, 69·2; H, 6·2. $C_{15}H_{16}O_4$ requires C, 69·2; H, 6·2%).

Manganese Dioxide Oxidation of iso*Tazettinol.*—*iso*Tazettinol (0·46 g.) and manganese dioxide (4 g.) in chloroform (50 ml.) were stirred for 6 hr. After being set aside overnight, manganese dioxide was filtered off and washed with chloroform. The combined filtrate and washings were extracted with 5% hydrochloric acid which removed some unchanged starting material (275 mg.). Concentration of the chloroform gave the *keto-lactone* (II; R, R′ = O, R″ = Me) (70 mg.), needles, m. p. 214—216° (decomp.) (from acetone or ethanol), $[\alpha]_D$ +250°

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(*c* 0·4 in EtOH), $\nu_{max.}$ 1730 (lactone), 1698 (ketone), and 1684 cm.$^{-1}$ (amide) (Found: C, 62·1; H, 4·6; N, 4·4. $C_{17}H_{15}O_6N$ requires C, 62·0; H, 4·6; N, 4·3%). The solid from the mother-liquors was chromatographed in benzene over acid-washed alumina. The first benzene eluate gave an additional crop (10 mg.) of the above keto-lactone, and the second benzene eluate afforded a substance (10 mg.), needles, m. p. 266—267° (Found: C, 62·4; H, 4·7), the structure of which is still to be elucidated. Further elution with chloroform gave the *hydroxy-lactone* (II; R = H, R′ = OH, R″ = Me) (15 mg.), needles, m. p. 207—209° (decomp.) (from ethanol), raised to 216—218° after drying *in vacuo* at 100°, $[\alpha]_D$ +235° (*c* 0·43 in EtOH), $\nu_{max.}$ 3390—3125 (OH), 1721 (lactone) and 1653 cm.$^{-1}$ (amide) in Nujol mull, and 3597 (OH), 1730 (lactone), and 1672 cm.$^{-1}$ (amide) in chloroform (Found: C, 61·4; H, 5·7; N, 4·3. $C_{17}H_{17}O_6N$ requires C, 61·6; H, 5·2; N, 4·2%). The keto-lactone (II; R, R′ = O, R″ = Me) was converted into 2-*p*-hydroxyphenyl-4 : 5-methylenedioxybenzyl alcohol, m. p. and mixed m. p. 186—188°, upon prolonged heating in 15% aqueous potassium hydroxide.

Hydrogenation of the Keto-lactone (II; R, R′ = O, R″ = Me).—(*a*) The keto-lactone (30 mg.) in ethanol (30 ml.) was hydrogenated over 10% palladium–carbon (50 mg.) for 3 hr. The crude product was chromatographed in benzene over acid-washed alumina. The first benzene eluate gave an oil (2 mg.). Further elution with benzene gave the *dihydro-keto-lactone* (III; R, R′ = O, R″ = Me) (25 mg.), prisms, m. p. 185—187° (from benzene), $\nu_{max.}$ 1733 (lactone), 1718 (ketone), and 1667 cm.$^{-1}$ (amide) (Found: C, 61·9; H, 5·3. $C_{17}H_{17}O_6N$ requires C, 61·6; H, 5·2%).

(*b*) The keto-lactone (30 mg.) in ethanol (30 ml.) was hydrogenated over 10% palladium–carbon for 4 days during daylight hours. Chromatography of the resulting product in benzene over acid-washed alumina furnished from a benzene eluate the dihydro-keto-lactone (15 mg.), m. p. and mixed m. p. 185—187° (from benzene), and the dihydro-alcohol (III; R = H, R′ = OH, R″ = Me) (10 mg.), m. p. and mixed m. p. 125—127° (from benzene–ligroin) from a methanol eluate.

Manganese Dioxide Oxidation of Dihydroisotazettinol.—Dihydro*iso*tazettinol (0·4 g.) in chloroform (35 ml.) and acetone (5 ml.) was stirred with manganese dioxide (4 g.) at room temperature for 15 hr. Manganese dioxide was removed and washed with chloroform, and the combined filtrate and washings were extracted with 5% hydrochloric acid to remove unchanged starting material (90 mg.). The residue from the chloroform solution was chromatographed in benzene over acid-washed alumina. The benzene eluate gave an oil, and the chloroform and the acetone eluates gave 2′-(*N-formyl-N-methylamino*)-4′-*hydroxy*-6 : 7-*methylenedioxy*-3-*oxoiso-chroman*-4-spiro-1′-cyclo*hexane* (III; R = H, R′ = OH, R‴ = Me) (0·18 g.), needles, m. p. 125—127° (from benzene), $[\alpha]_D$ +75° (*c* 0·24 in EtOH), $\nu_{max.}$ 3472 and 3225 (OH), 1730 (lactone), and 1686 and 1667 cm.$^{-1}$ (amide) (Found: C, 59·7; H, 6·0. $C_{17}H_{19}O_6N,\frac{1}{2}H_2O$ requires C, 59·7; H, 5·9%). Hydrolysis of this (40 mg.) in 10% potassium hydroxide (2 ml.) on a water-bath for 3 hr., followed by lactonisation in dilute sulphuric acid, gave an *amine* (III; R = H, R′ = OH, R″ = Me, H in place of CHO) (18 mg.), needles, m. p. 185—187° (from ethanol), $\nu_{max.}$ 3521 (OH, NH), and 1724 cm.$^{-1}$ (lactone) (Found: C, 62·7; H, 6·3. $C_{16}H_{19}O_5N$ requires C, 62·9; H, 6·3%).

Reduction of O-*Demethyldihydroisotazettamide* (III; R = H, R′ = OH, R″ = Me).—The amide (0·3 g.) and lithium aluminium hydride (0·25 g.) were heated in tetrahydrofuran (10 ml.) under reflux for 4 hr. The crude oily base isolated was heated in 5% sulphuric acid (20 ml.) for 1·5 hr. Basification and extraction with ether gave an oil (0·2 g.) which was chromatographed in benzene over alumina. The first benzene eluate did not give a crystalline picrate. The second benzene eluate and the benzene–chloroform (1 : 1) eluate gave the *picrate* of an amino-alcohol (V; R = H, R′ = OH) which when crystallised from methanol formed needles (0·13 g.), m. p. 204—207°, raised to 220—222° (decomp.) by drying *in vacuo* (Found: C, 50·8; H, 5·0; N, 10·3. $C_{17}H_{23}O_4N,C_6H_3O_7N_3,\frac{1}{2}H_2O$ requires C, 50·9; H, 5·0; N, 10·3%). The free base regenerated from the picrate was converted into its *carbonate*, m. p. 194° (prisms from benzene) [Found: C, 62·6; H, 6·9. $(C_{17}H_{23}O_4N)_2H_2CO_3$ requires C, 62·5; H, 7·1%]. The 3 : 5-*dinitrobenzoate* of the base formed orange yellow prisms, m. p. 236—238° (from chloroform–ethanol) (Found: C, 57·6; H, 5·0; N, 8·5. $C_{24}H_{23}O_9N_3$ requires C, 58·0; H, 4·6; N, 8·5%).

Emde Degradation of the Amino-alcohol (V; R = H, R′ = OH).—The foregoing amino-alcohol (0·12 g.) regenerated from its picrate gave with methyl iodide in methanol the methiodide which was immediately converted into its chloride by shaking it with an excess of silver chloride.

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The chloride in water (5 ml.) was heated with 5% sodium amalgam (30 g.) on a water-bath for 6 hr. The oil which separated was extracted with chloroform, which was washed with 5% hydrochloric acid and water, dried, and evaporated, to give a neutral product which was chromatographed in benzene–ligroin (1 : 1) over acid-washed alumina. Elution with benzene–ligroin (1 : 1) and benzene gave an oil (8 mg.). The second benzene eluate afforded *4'-hydroxy-6 : 7-methylenedioxyisochroman-4-spiro-1'-cyclohexane* (VI; R = H, R' = OH) (20 mg.) which crystallised from ligroin, then from benzene as prisms, m. p. 146—148° (Found: C, 68·3; H, 6·6. $C_{15}H_{18}O_4$ requires C, 68·7; H, 6·9%). The 3 : 5-dinitrobenzoate had m. p. 278° (pale yellow needles from chloroform–ethanol).

2 : *4-Dicyano-1-imino-4-phenylcyclohexane* (IX; R = NH, R' = CN).—(*a*) To a stirred solution of benzyl cyanide (2 g.) and β-bromopropionitrile (4·8 g.) in toluene (40 ml.) powdered sodium amide (0·8 g.) was added in portions. Stirring was continued at room temperature for 8 hr., then under reflux for 2 hr. After cooling, the excess of sodium amide was destroyed with acetic acid, the precipitated sodium acetate removed by filtration, and the toluene washed with aqueous sodium carbonate, then water, dried, and evaporated under reduced pressure to give the *ketimine* (4 g.) which crystallised from ethanol as needles, m. p. 145—146° (Found: C, 75·3; H, 6·0. $C_{14}H_{13}N_3$ requires C, 75·3; H, 5·9%).

(*b*) Sodium amide (1 g.) was added to γ-cyano-γ-phenylpimelonitrile [13] (2 g.) in toluene (30 ml.), and the mixture refluxed for 5 hr. On working up of the mixture as described above, the same ketimine (0·8 g.) was obtained.

Methyl 3-Cyano-6-oxo-3-phenylcyclohexanecarboxylate (IX; R = O, R' = CO_2Me).—Sodium amide (2·5 g.) was added in portions with stirring to a mixture of benzyl cyanide (0·9 g.), methyl β-bromopropionate (3 g.), and toluene (30 ml.). Stirring was continued at room temperature for 24 hr., then under reflux for 4 hr. After cooling, a little acetic acid and then water were added and the toluene layer was washed with aqueous sodium carbonate, dried, and evaporated to dryness to give the *cyclohexanone-ester* (1·5 g.). It crystallised from benzene as needles, m. p. 90—91·5° (Found: C, 70·3; H, 5·9; N, 5·5. $C_{15}H_{15}O_3N$ requires C, 70·0; H, 5·9; N, 5·4%).

Acidic Hydrolysis of the Keto-ester (IX; R = O, R' = CO_2Me).—The keto-ester (0·1 g.) was refluxed in 2% ethanolic sodium hydroxide (20 ml.) containing water (5 ml.) for 4 hr. The mixture was concentrated and the residue in dilute hydrochloric acid was extracted with ether. The organic layer was extracted with aqueous sodium carbonate which was made acid and extracted again with ether. The ethereal extract was dried and evaporated to furnish *γ-cyano-γ-phenylpimelic acid* (0·1 g.), m. p. 167—168°, $\nu_{max.}$ 2237 (CN), 2577—2725 and 1724 cm.$^{-1}$ (CO_2H) (from methanol) (Found: C, 64·4; H, 5·8. $C_{14}H_{15}O_4N$ requires C, 64·4; H, 5·8%). This was not identical (mixed m. p. and infrared spectra) with α-2-carboxyethyl-α-phenylglutarimide.[7]

4-Cyano-4-phenylcyclohexanone (IX; R = O, R' = H).—(*a*) The above ketimine (0·5 g.) was heated in acetic acid (15 ml.) containing 30% sulphuric acid (10 ml.) on the water-bath for 10 hr. After cooling, water (20 ml.) was added, and the whole was extracted with benzene which in turn was washed with aqueous sodium carbonate, water, dried, and evaporated to dryness, to give a residue (60 mg.). This was passed in benzene through a column of alumina, affording the *cyano-ketone* (30 mg.), m. p. 114—115°, needles from benzene (Found: C, 78·1; H, 6·5. $C_{13}H_{13}ON$ requires C, 78·4; H, 6·6%).

(*b*) The β-keto-ester obtained as above (0·1 g.) was refluxed in ethanol (20 ml.) and concentrated hydrochloric acid (3 ml.) for 4 hr. The mixture was concentrated under reduced pressure to 10 ml., diluted with water (30 ml.), and extracted with ether. The ether extracts were washed with aqueous sodium carbonate and water, dried, and evaporated to dryness. The residue (70 mg.) gave the ketone, m. p. and mixed m. p. 114—115°, needles from benzene.

γ-Cyano-γ-(3 : 4-methylenedioxyphenyl)pimelonitrile (XI).—(*a*) 30% Methanolic Triton B (0·2 g.) was added dropwise to a stirred mixture of 3 : 4-methylenedioxybenzyl cyanide (1·6 g.) and acrylonitrile (1·5 g.) during 15 min. at 30—40°, the mixture becoming dark brown and viscous. After being heated on the water-bath for 30 min., the mixture was taken up in chloroform (100 ml.), washed with dilute hydrochloric acid, aqueous sodium carbonate, and water, dried, and evaporated to dryness under reduced pressure. The residue crystallised, giving the *trinitrile* as prisms (2·5 g.). After crystallisation from methanol, it had m. p. 91—93° (Found: C, 67·3; H, 4·7; N, 15·3. $C_{15}H_{13}O_2N_3$ requires C, 67·4; H, 4·9; N, 15·7%).

[13] Bruson and Riener, *J. Amer. Chem. Soc.*, 1943, **65**, 23.

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(*b*) 30% Methanolic Triton B (0·4 g.) in *tert.*-butyl alcohol (5 ml.) was added dropwise to a stirred solution of 3 : 4-methylenedioxybenzyl cyanide (3 g.) and acrylonitrile (3 g.) in *tert.*-butyl alcohol (10 ml.) at 35—45°. After 1 hour's stirring, the mixture was concentrated, and the resulting residue was taken up in ethylene dichloride, washed with dilute hydrochloric acid, aqueous sodium carbonate, and water, dried, and evaporated to dryness, to give the pimelonitrile (5 g.) which crystallised from methanol as prisms, m. p. and mixed m. p. 91—93°.

α-2-*Carboxyethyl*-α-(3 : 4-*methylenedioxyphenyl*)*glutarimide* (XIII; R = R′ = H).—γ-Cyano-γ-(3 : 4-methylenedioxyphenyl)pimelonitrile (2·7 g.) in acetic acid (15 ml.) containing concentrated hydrochloric acid (30 ml.) and water (5 ml.) was heated on the water-bath for 2·5 hr. during which the mixture became dark brown. On cooling, crystals separated which were collected and recrystallised from aqueous ethanol, to give the *imidocarboxylic acid*, m. p. 220—221° (Found: C, 58·7; H, 4·8; N, 4·7. $C_{15}H_{15}O_6N$ requires C, 59·0; H, 5·0; N, 4·6%), $\nu_{max.}$ 3077—3175 (NH), 2584—2740 (OH of carboxylic acid), 1656, 1712, 1730 cm.$^{-1}$ (CO).

Treatment of the Imidocarboxylic Acid (XIII; R = R′ = H) *with Diazomethane.*—Excess of ethereal diazomethane was added to a suspension of the imidocarboxylic acid (3 g.) in ether (50 ml.) and methanol (10 ml.). This was kept overnight at room temperature, then a little acetic acid was introduced into the mixture to destroy the excess of diazomethane and the mixture was washed with aqueous sodium carbonate, dried, and evaporated to give α-2-*methoxycarbonylethyl*-N-*methyl*-α-(3 : 4-*methylenedioxyphenyl*)*glutarimide*, b. p. 200—230°(bath)/0·03 mm. (Found: OMe, 9·0. $C_{17}H_{19}O_6N$ requires OMe, 9·3%).

Treatment of the Ester (XIII; R = R′ = Me) *with Sodium Methoxide.*—The above ester (3 g.) and sodium methoxide (2 g.) were refluxed in benzene (30 ml.) for 2 hr. The mixture was then acidified with dilute hydrochloric acid, and the benzene layer washed with aqueous sodium carbonate, dried, and evaporated under reduced pressure to give an oil (2·3 g.). This was heated in ethanol (50 ml.) and concentrated hydrochloric acid (20 ml.) under reflux for 10 hr., which was next concentrated under reduced pressure to 15 ml., diluted with water (80 ml.), and extracted with ether. The ethereal extracts were washed with aqueous sodium carbonate and water, dried, and evaporated to dryness and the residue was chromatographed in benzene over alumina. The benzene eluate gave the 1-(3 : 4-*methylenedioxyphenyl*)-N-*methyl*-4-*oxo*cyclo*hexanecarboxyamide* (XIV; R = H) (25 mg.), m. p. 151—152°, as plates from benzene (Found: C, 65·3; H, 6·1; N, 5·1. $C_{15}H_{17}O_4N$ requires C, 65·4; H, 6·2; N, 5·1%), $\nu_{max.}$ 3413 (NH), 1681, 1718 cm.$^{-1}$ (CO). The 2 : 4-*dinitrophenylhydrazone*, m. p. 138—141°, formed needles from ethanol (Found: C, 55·0; H, 5·0. $C_{21}H_{21}O_7N_5$ requires C, 55·4; H, 4·7%).

2 : 4-*Dicyano*-1-*imino*-4-(3 : 4-*methylenedioxyphenyl*)cyclo*hexane* (XVI).—γ-Cyano-γ-(3 : 4-methylenedioxyphenylpimelonitrile (XI) (1 g.) and sodium amide (0·7 g.) in toluene (20 ml.) were heated under reflux for 6 hr. A little acetic acid and then water were added to the mixture, and the toluene layer was washed with aqueous sodium carbonate and water, dried, and evaporated to dryness under reduced pressure. The residue, which solidified, crystallised from benzene to give the *ketimine* (0·8 g.) as needles, m. p. 191—193° (Found: C, 67·1; H, 4·7; N, 15·6. $C_{15}H_{12}O_3N_2$ requires C, 67·4; H, 4·9; N, 15·7%).

Methyl γ-*Cyano*-γ-(3 : 4-*methylenedioxyphenyl*)*pimelate* (XII; R = Me).—30% Methanolic Triton B (1 g.) in *tert.*-butyl alcohol (2 ml.) was added dropwise to a stirred mixture of 3 : 4-methylenedioxybenzyl cyanide (3·2 g.), methyl acrylate (3·5 g.), and *tert.*-butyl alcohol (10 ml.) during 30 min. at 65—70°. The mixture was heated under reflux for 2 hr. and then the solvent was removed by distillation. The resulting oil was taken up in chloroform, washed with dilute hydrochloric acid, aqueous sodium carbonate, and water, dried, and evaporated to dryness. The residue (6·5 g.) was fractionated by distillation into two portions; the first fraction (1 g.), b. p. 190—210°(bath)/0·01 mm., was discarded; the second fraction (4·8 g.), b. p. 245—255° (bath)/0·005 mm., crystallised overnight. Recrystallisation from ethanol gave the *ester* (XII; R = Me), prisms, m. p. 45—46° (Found: C, 61·5; H, 5·8; N, 4·2; OMe, 18·3. $C_{17}H_{19}O_6N$ requires C, 61·3; H, 5·8; N, 4·2; OMe, 18·6%).

Methyl 5-*Cyano*-5-(3 : 4-*methylenedioxyphenyl*)-2-*oxo*cyclo*hexanecarboxylate* (XV; R = CO_2Me).—The methyl cyanopimelate (4·5 g.) obtained as above and sodium hydride (0·4 g.) were heated in toluene (100 ml.) containing a few drops of methanol under reflux under nitrogen for 4 hr. A little acetic acid was added to the mixture to destroy the excess of sodium hydride, and the mixture was shaken with aqueous sodium carbonate and water, dried, and evaporated under reduced pressure. The residue crystallised from ethanol, to give the cyclo*hexanone-ester*

(3·2 g.) as needles, m. p. 136—137° (Found: C, 63·8; H, 5·0; N, 4·5. $C_{16}H_{15}O_5N$ requires C, 63·8; H, 5·0; N, 4·7%), $\nu_{max.}$ 2242 (CN) and 1675 cm.$^{-1}$ (CO).

γ-Cyano-γ-(3 : 4-methylenedioxyphenyl)pimelic Acid (XII; R = H).—Methyl γ-cyano-γ-(3 : 4-methylenedioxyphenyl)pimelate was hydrolysed in the usual way in alkali to give the *acid*, m. p. 178—179, needles (from ethanol) (Found: C, 59·3; H, 5·1; N, 4·5. $C_{15}H_{15}O_6N$ requires C, 59·0; H, 5·0; N, 4·6%).

4-*Cyano*-4-(3 : 4-*methylenedioxyphenyl*)cyclo*hexanone* (XV; R = H).—(*a*) The imido-carboxylic acid (XIII; R = R′ = H) (2 g.) in acetic anhydride (30 ml.) was heated under reflux for 8 hr. After evaporation of the mixture to dryness under reduced pressure, the residue was kept at 200° under reduced pressure for 20 min. The product was taken up in chloroform, washed with aqueous sodium carbonate, dried, and concentrated to dryness to give an oil (0·4 g.) which was distilled *in vacuo* to give a fraction, b. p. 170—175° (bath)/0·01 mm. This was chromatographed in benzene over alumina, and the eluate furnished 4-*cyano*-4-(3 : 4-*methylenedioxyphenyl*)cyclo*hexanone* as needles (50 mg.), m. p. 134—135°, from benzene (Found: C, 69·4; H, 5·3; N, 5·9. $C_{14}H_{13}O_3N$ requires C, 69·1; H, 5·4; N, 5·8%), $\nu_{max.}$ 2252 (CN) and 1724 cm.$^{-1}$ (CO). The 2 : 4-*dinitrophenylhydrazone* had m. p. 220—223° (from ethanol) (Found: C, 56·9; H, 4·2. $C_{20}H_{17}O_6N_5$ requires C, 56·7; H, 4·1%).

(*b*) The *cyclo*hexanone-ester (XV; R = CO_2Me) (10 g.) was refluxed for 10 hr. in ethanol (200 ml.), concentrated hydrochloric acid (100 ml.), and 25% sulphuric acid (10 ml.). The mixture was concentrated to 100 ml., diluted with water (400 ml.), and extracted with ether. This extract was washed with aqueous sodium carbonate and water, dried, and evaporated to dryness to give a solid (6·5 g.) which was crystallised from benzene, affording the ketone (XV; R = H) (5 g.), m. p. and mixed m. p. 134—135°. The mother-liquor was chromatographed (*A*) in benzene over alumina. The first benzene eluate gave the *diethyl ketal* (XVIII; R = Et) (0·5 g.) of the ketone (XV; R = H); this formed needles, m. p. 127—129° from ethanol (Found: C, 68·2; H, 7·2; N, 4·6; OEt, 28·1. $C_{18}H_{23}O_4N$ requires C, 68·1; H, 7·3; N, 4·4; OEt, 28·4%); it was identical with the ketal prepared from the ketone (XV; R = H) in ethanol in the presence of toluene-*p*-sulphonic acid. The later fractions from the chromatogram (*A*) eluted with the same solvent gave the ketone (0·5 g.).

(*c*) The ketimine (XVI) (1 g.) obtained above was heated on a water-bath for 10 hr. in ethanol (25 ml.) containing 30% aqueous sulphuric acid (15 ml.). The mixture was concentrated to 25 ml., diluted with water, and extracted with ether. The ethereal extract was washed with aqueous sodium carbonate and water, dried, and evaporated, to give an oil (70 mg.) which was chromatographed in benzene over alumina. This afforded the cyano-ketone (XV; R = H) (30 mg.), m. p. and mixed m. p. 134—135° (from carbon tetrachloride).

4-*Cyano*-4-(3 : 4-*methylenedioxyphenyl*)cyclo*hexanol* (XVII).—A suspension of sodium borohydride (1 g.) in methanol (50 ml.) was added in portions to 4-cyano-4-(3 : 4-methylenedioxyphenyl)*cyclo*hexanone (XV; R = H) (4 g.) in methanol (150 ml.) at 0°. After being kept overnight, the mixture was evaporated under reduced pressure, diluted with water, and extracted with ether. The ethereal extract was washed with dilute hydrochloric acid, aqueous sodium carbonate, and water, dried, and evaporated to give a solid, m. p. 96—105° which when crystallised from benzene gave 4-*cyano*-4-(3 : 4-*methylenedioxyphenyl*)cyclo*hexanol* (2 g.), prisms, m. p. 121—122° (Found: C, 69·0; H, 6·1; N, 5·6. $C_{14}H_{15}O_3N$ requires C, 68·6; H, 6·2; N, 5·7%), $\nu_{max.}$ 3534 (OH) and 2247 cm.$^{-1}$ (CN). The mother-liquor from the *cyclo*hexanol was chromatographed over alumina. The first benzene eluate gave 4-*cyano*-4-(3 : 4-*methylenedioxyphenyl*)cyclo*hexanone dimethyl ketal* (XVIII; R = Me) (1 g.), m. p. 107—108° (from methanol) [Found: C, 66·4; H, 6·5; N, 4·8; OMe, 21·4. $C_{14}H_{13}O_2N(OMe)_2$ requires C, 66·4; H, 6·6; N, 4·8; OMe, 21·4%]. This was identical with the ketal prepared from the ketone (XV; R = H) and toluene-*p*-sulphonic acid in methanol. The second benzene eluate gave the *cyclo*hexanol (XVII) (0·5 g.). The *acetyl derivative* of the *cyclo*hexanol formed needles, m. p. 161—162°, from ethanol (Found: C, 66·7; H, 5·9; N, 5·1. $C_{16}H_{17}O_4N$ requires C, 66·9; H, 6·0; N, 4·9%), $\nu_{max.}$ 2247 (CN) and 1733 cm.$^{-1}$ (CO) in a KBr disc. The *toluene-p-sulphonate* was obtained when the *cyclo*hexanol (0·2 g.) and toluene-*p*-sulphonyl chloride (0·17 g.) were kept overnight in pyridine (4 ml.) at 30°; the mixture was poured into water and extracted with chloroform, and the chloroform extract washed with dilute hydrochloric acid and evaporated; the residue crystallised from ethanol as needles, m. p. 162—163° (Found: C, 63·0; H, 5·1; N, 3·4. $C_{21}H_{21}O_5NS$ requires C, 63·2; H, 5·3; N, 3·5%).

It was later found that the formation of the ketal (XVIII; R = Me) in the course of the

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sodium borohydride reduction of the ketone could be avoided when tetrahydrofuran was used as a solvent in place of methanol, giving the *cyclo*hexanol (XVII) in an excellent yield.

*4-Hydroxy-1-(3 : 4-methylenedioxyphenyl)*cyclo*hexanecarboxylic Acid* (XIX).—4-Cyano-4-(3 : 4-methylenedioxyphenyl)*cyclo*hexanol (0·3 g.) and potassium hydroxide (4·5 g.) were boiled under reflux in diethylene glycol (16 ml.) and water (6 ml.) for 8 hr. A crystalline precipitate appeared after 1 hr., but soon disappeared with liberation of ammonia. After cooling, the mixture was diluted with water (100 ml.) and filtered; the acid (XIX) was precipitated on addition of hydrochloric acid. Crystallisation from ethanol gave the *acid* (0·25 g.), m. p. 220—222° (decomp.), $\nu_{max.}$ 3378 (OH) and 1686 cm.$^{-1}$ (CO_2H) (Found: C, 63·8; H, 6·4. $C_{14}H_{16}O_5$ requires C, 63·6; H, 6·1%). Extraction of the mother-liquors with ethyl acetate yielded a little more acid (0·05 g.).

*4-Hydroxy-1-(3 : 4-methylenedioxyphenyl)*cyclo*hexanecarboxylic Lactone* (XX; R = H).—The hydroxy-acid (XIX) (30 mg.) was refluxed in acetic anhydride (5 ml.) for 5 hr. Evaporation under reduced pressure gave the *lactone*, m. p. 219—220°, prisms (from ethanol), $\nu_{max.}$ 1739 cm.$^{-1}$ (six-membered lactone) (Found: C, 68·5; H, 5·7. $C_{14}H_{14}O_4$ requires C, 68·3; H, 5·7%). The lactone regenerated the hydroxy-acid on hydrolysis in alkali.

*1-(2-Chloromethyl-4 : 5-methylenedioxyphenyl)-4-hydroxy*cyclo*hexanecarboxylic Lactone* (XX; R = CH_2Cl).—(*a*) The hydroxy-acid (XIX) (0·5 g.) and paraformaldehyde (0·5 g.) were heated with stirring in acetic acid (10 ml.) containing concentrated hydrochloric acid (6 ml.) at 70—75° for 10 hr. The mixture was evaporated to dryness under reduced pressure and the residue taken up in chloroform. The chloroform solution was washed with aqueous sodium carbonate and water, dried, and evaporated to give a dark brown oil (0·35 g.) which was chromatographed in benzene over acid-washed alumina. The first fractions eluted with benzene gave the *chloromethyl derivative* (XX; R = CH_2Cl) (0·15 g.). It crystallised from ethanol as leaflets, m. p. 143—145°, $\nu_{max.}$ 1745 cm.$^{-1}$ (six-membered lactone) (Found: C, 61·6; H, 5·5; Cl, 11·4. $C_{15}H_{15}O_4Cl$ requires C, 61·1; H, 5·1; Cl, 12·0%). Later fractions eluted with chloroform gave a substance (50 mg.), m. p. 215—216°, which was not investigated further.

(*b*) The lactone (XX; R = H) (0·5 g.) was similarly chloromethylated, and the chloromethyl derivative, m. p. and mixed m. p. 143—145° (0·2 g.), was obtained along with the starting material (0·15 g.) and the unidentified product, m. p. 215—216°.

The Hydroxy-lactone (XXI).—The chloromethyl-lactone (XX; R = CH_2Cl) (0·1 g.) was heated in 10% aqueous sodium hydroxide (10 ml.) on the water-bath for 10 hr. The mixture was acidified with dilute sulphuric acid, then heated at 100° for a further 8 hr. The mixture was repeatedly extracted with ether and the ethereal extracts were washed with aqueous sodium carbonate and evaporated to dryness, to give the *4′-hydroxy-6 : 7-methylenedioxy-3-oxo*iso*chroman-4*-spiro-1′-cyclo*hexane* (XXI) which crystallised from ethanol as prisms (40 mg.), m. p. 156—157°, $\nu_{max.}$ 3448 (OH) and 1724 cm.$^{-1}$ (six-membered lactone) (Found: C, 65·2; H, 5·6. $C_{15}H_{16}O_5$ requires C, 65·2; H, 5·8%).

*4′-Hydroxy-6 : 7-methylenedioxy*iso*chroman-4*-spiro-1′-cyclo*hexane* (VI; R = H, R′ = OH).—The hydroxy-lactone (XXI) (0·1 g.) and lithium aluminium hydride (0·1 g.) were boiled under reflux in tetrahydrofuran (8 ml.) for 8 hr. The mixture was treated with a little water, then filtered, and the precipitate washed with methanol. The filtrate and washings were combined and concentrated to dryness, to give an oil which was heated in 3% sulphuric acid (20 ml.) on the water-bath for 3 hr. and then extracted with ether. The ethereal extracts were evaporated and the residue (60 mg.) was chromatographed in benzene over acid-washed alumina to afford the iso*chroman* (VI; R = H, R′ = OH), m. p. 146—147°, plates (from benzene) (Found: C, 68·3; H, 6·6. $C_{15}H_{18}O_4$ requires C, 68·7; H, 6·9%), identical in m. p., mixed m. p., and infrared spectrum with the Emde product derived from *iso*tazettinol described above.

The product (90 mg.) and toluene-*p*-sulphonyl chloride (0·1 g.) in pyridine (3 ml.) were kept overnight at 35°. After addition of crushed ice (10 g.), the mixture was extracted with chloroform, which was washed with dilute hydrochloric acid, aqueous sodium carbonate, and water, dried, and evaporated to dryness. The residue, crystallised from ethanol, gave the *toluene-p-sulphonate* (128 mg.) as needles, m. p. 180—181° (Found: C, 63·4; H, 6·0. $C_{22}H_{24}O_6S$ requires C, 63·5; H, 5·8%).

*4′-Methoxy-6 : 7-methylenedioxy*iso*chroman-4*-spiro-1′-cyclo*hexane* (VI; R = OMe, R′ = H).—The above toluene-*p*-sulphonate (0·1 g.) was heated with a solution from sodium (3 g.) in methanol (70 ml.) under reflux for 10 hr., then evaporated under reduced pressure. Water

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was added and the mixture extracted with ether. This extract was washed with dilute hydrochloric acid and water, dried, and concentrated to an oil (60 mg.). This was chromatographed in benzene on alumina and eluted with benzene. The first fraction afforded 6 : 7-*methylenedioxy*iso*chroman*-4-spiro-1′-cyclo*hex*-3′-*ene* (XXIII) (32 mg.) which crystallised from ethanol as prisms, m. p. 101—102° (Found: C, 73·7; H, 6·8. $C_{15}H_{16}O_2$ requires C, 73·8; H, 6·6%). The second fraction gave 4′-*methoxy*-6 : 7-*methylenedioxy*iso*chroman*-4-spiro-1′-cyclo*hexane* (20 mg.) which, when dissolved in a little ethanol and seeded with a sample, m. p. 56—58°, of the same structure obtained previously by degradation of tazettamide, formed prisms and had m. p. 52°. But another recrystallisation from the same solvent raised the m. p. to 90° and once the higher-melting polymorph had been obtained the lower-melting form was never recovered during recrystallisation. The compound derived from natural sources showed also the same m. p. when seeded with the synthetic higher-melting form and mixed m. p. showed no depression. The infrared spectra were also identical (Found: C, 69·2; H, 7·5. $C_{16}H_{20}O_4$ requires C, 69·5; H, 7·3%).

6 : 7-*Methylenedioxy*iso*chroman*-4-spirocyclo*hexane* (VI; R = R′ = H).—The *spirocyclo*hexene (XXIII) (4 mg.) was hydrogenated in ethanol (5 ml.) in the presence of platinic oxide (7 mg.). The filtered solution was evaporated and the residue was chromatographed in benzene over alumina. The benzene eluate gave the *spirocyclo*hexane (VI; R = R′ = H) as prisms, m. p. 54—55° which did not depress the m. p. of the product obtained by Emde degradation of (V; R = R′ = H).

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Osaka, Japan. [*Received, November 21st*, 1958.]

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283. *Ion-exchange Studies of Phosphates. Part III.*[1] *Complex Formation between Tervalent Metals and Orthophosphoric Acid.*

By J. A. R. Genge and J. E. Salmon.

Equilibrium batch experiments with various tervalent-metal (Al, Fe, Ti, In, Sc, Yb, Er, Nd, and La) forms of a strong cation-exchange resin and orthophosphoric and perchloric acid solutions are used to assess the degree of complex formation. Where possible, comparison is made with conclusions based on the results of pH titrations of the metal chloride solutions with phosphoric acid.

With perchloric acid there is little sign of complex formation, but with phosphoric acid there is found a regular variation in the degree of complex formation with the ionic radius (non-hydrated) of the metal. There is an optimum ionic radius for complex formation of approximately 0·7 Å, corresponding closely to that of titanium(III) and a gradual decrease at higher or lower radii.

An explanation of this is offered in terms of the ease of formation of a four-membered chelate ring, and it is shown that the optimum radius of 0·7 Å is that required to give the least strain and the minimum distortion of bond angles.

Previously we showed[1] that the degree of complex formation between metals and orthophosphoric and other acids could be estimated from results of equilibrium batch experiments with the metal form of a strong cation-exchange resin and the acid. This suggested the possibility of comparing the tendencies to complex formation of a number of metals of the same valency with phosphoric acid and covering a wide range of ionic radii. Results obtained in this way with many metals and with both phosphoric and perchloric acids are given.

[1] Part II, Genge and Salmon, *J.*, 1957, 256.

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Another method which has been used to estimate the degree of complex formation is that of pH titrations with use of the complexing acid and a suitable solution of the metal.[2] Under conditions where the complexes formed are soluble, results so obtained are used to verify those obtained by the ion-exchange method.

Experimental

Resins.—The strong cation-exchanger, Zeo-Karb 225 (approximately 10% cross-linked), of bead size 20—40 mesh was used for all the batch experiments. The metal form of the resin was prepared in each case as previously described.[1] With each batch, the total metal capacity was determined on 0·500 g. samples by complete elution with 2N-hydrochloric acid and analysis of the eluate. The total hydrogen capacity of the same sample was then determined as previously described [3] and the resin was used only if these two capacities were very nearly equal, showing complete loading.

Procedure.—For the batch experiments, 0·500 g. samples of the metal form of the resin were left, with occasional gentle swirling, for 7 days at room temperature (20° ± 3°) (which proved sufficient for attainment of equilibria) with 50 ml. of the acid of known pH.[1] A 25 ml. portion was then analysed for the metal. Analysis for La, Nd, Yb, and Er in the presence of phosphate proved difficult and it was found more convenient in these cases to filter off the resin into a small column (10 cm. × 1 cm. diam. with a sealed-in grade 2 sintered-glass disc) and wash thoroughly. The metal on the resin was then eluted with 2N-hydrochloric acid and determined in the eluate. The amount originally removed from the resin by the acid was then obtained by difference. In all cases, the final results are given as the percentage of the metal originally present on the resin which had been removed by the acid. All work with titanium(III) had to be carried out in an inert atmosphere, and an apparatus and technique were developed. A wide-necked glass cylinder (250 ml.) was fitted with a rubber bung carrying a dropping funnel, two inlet tubes to the top of the cylinder, and an outlet tube from the bottom. One inlet tube was for nitrogen and the other, which contained 0·500 g. of the hydrogen form of the resin supported on a glass-wool plug, was connected through a glass junction to two burettes. At the start of each experiment, the whole apparatus was filled with water and then emptied by passing nitrogen. Acidified titanous chloride, which is reasonably stable towards atmospheric oxidation, was run in from one burette and diluted with water from the other before reaching the resin. When an excess had been used, water alone was passed through to wash the resin. The collecting cylinder was then cleaned by alternately filling with water and blowing out with nitrogen. The resin was then dropped into the cylinder by pushing away the glass wool with a nickel wire, and 50 ml. of acid were added, and left for 7 days as in the normal batch experiments. For analysis, it was satisfactory if 25 ml. of the solution was rapidly withdrawn with a pipette and transferred immediately to an excess of iron alum solution.

pH *Titrations.*—The method used was that described by Holroyd and Salmon [2] but, for this work, *ca.* 0·75M-phosphoric acid was added in small quantities from a 5 ml. burette to 50 ml. of the metal chloride solution *ca.* 0·05M in metal. The pH was measured originally and after each addition on a pH meter with a glass electrode–calomel electrode system. pH values were converted to hydrogen-ion concentrations after the method of Holroyd and Salmon [2] and the quotient $[H_3PO_4]/[M]$ was plotted both against pH and against $\Delta[H]/[M]$, allowance being made in all cases for the increase in volume of the solution due to the addition of the phosphoric acid.

The titrations were carried out with iron(III), titanium(III), aluminium, and indium and also with potassium as a non-complexing system.

Analysis.—Titanium(III) was determined by addition of excess of ferric alum solution and subsequent titration of the ferrous iron with standard potassium dichromate, sodium diphenylaminesulphonate being used as indicator. Iron(III) was also determined by titration with standard dichromate after reduction to ferrous iron.

Aluminium and scandium were estimated by addition of excess of standard ethylenediaminetetra-acetic acid, and back-titration of the excess with standard zinc sulphate in 50% ethanol solution at pH 4·5 with dithizone as indicator.[4] Indium, lanthanum, neodymium,

[2] Holroyd and Salmon, *J.*, 1956, 269.
[3] Salmon, *J.*, 1953, 2644.
[4] Lukaszewski, Redfern, and Salmon, *Lab. Practice*, 1957, **6**, 390.

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ytterbium, and erbium were determined by a similar back-titration method, but in aqueous solution at pH 10·0 with Eriochrome Black T as indicator.[5]

Results and Discussion

The amount of each metal removed from the resin with phosphoric and perchloric acids at pH 0·25, 0·50, 0·75, and 1·00 are shown in Fig. 1 where the percentage of metal removed is plotted against the (non-hydrated) ionic radius.

Published tables of ionic radii are incomplete and, for this work, the values for Ti, Fe, Al, La, In, and Sc are taken from the list obtained theoretically by Pauling.[6] The remainder, for Nd, Yb, and Er, not given by Pauling, are taken from a list by Goldschmidt.[7] An increment of 0·6, which is a reasonably constant difference between the Pauling and Goldschmidt series, has been added to the latter values to bring them into line with the others.

Curves obtained with perchloric acid being considered first, these show clearly that there is little or no tendency to form complex ions. There is a steady drop in the

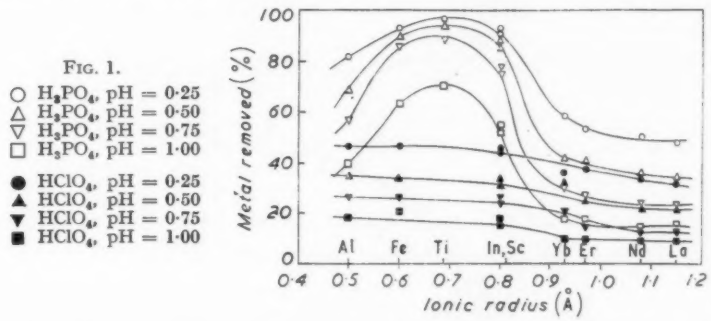

Fig. 1.

○ H_3PO_4, pH = 0·25
△ H_3PO_4, pH = 0·50
▽ H_3PO_4, pH = 0·75
□ H_3PO_4, pH = 1·00
● $HClO_4$, pH = 0·25
▲ $HClO_4$, pH = 0·50
▼ $HClO_4$, pH = 0·75
■ $HClO_4$, pH = 1·00

percentage of metal removed by the acid at any given pH with increase in ionic radius. This is to be expected since the smallest ion will be the most heavily hydrated and therefore the least firmly held on the resin. The curves obtained with phosphoric acid, on the other hand, show the occurrence of considerable complex formation, particularly with the metals of smaller ionic radius. Thus, with Al, Fe, Ti, In, and Sc, a high percentage of metal is removed and the curve shows a maximum at approximately 0·7 Å corresponding most closely to the ionic radius of titanium. The rare-earth metals, with larger ionic radii, show a lower removal but again the expected drop with increase in ionic radius is apparent.

The curves in Fig. 2 show the results of the pH titrations with titanium, iron, aluminium, and indium together with those of potassium for comparison. These results are substantially in agreement with those obtained in the ion-exchange experiments and, in both sets of results, the degree of complex formation is in the order Ti > Fe > In > Al. Further, the ion-exchange experiments show that this order is the same over a wide range of pH values. Previous work[1,8c] has indicated that the formation of chloro-complexes is likely to be very slight under these conditions.

In the ion-exchange experiments, the complexes formed will tend to be anionic and mononuclear.[9] Further, there are never more than three phosphate groups associated

[5] Genge and Salmon, *Lab. Practice*, 1957f **6**, 695.
[6] Pauling, *J. Amer. Chem. Soc.*, 1927, **49**, 765.
[7] Goldschmidt, *Trans. Faraday Soc.*, 1929, **25**, 253.
[8] (*a*) Holroyd and Salmon, *J.*, 1957, 959; (*b*) Holroyd, Jameson, Odell, and Salmon, *J.*, 1957, 3239; (*c*) Salmon and Wall, *J.*, 1958, 1128; (*d*) Brownlow, Salmon, and Wall, unpublished work.
[9] Jameson and Salmon, (*a*) *J.*, 1954, 28; (*b*) *J.*, 1954, 4013; (*c*) *J.*, 1955, 360; (*d*) Salmon and Wall, unpublished work.

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with one metal atom of co-ordination number six,[9] which suggests that the complexes are of a chelate type with the phosphate acting as a bidentate ligand. Over the pH range used in the titration experiments (1·0—3·0) the complex ions will tend to be cationic and binuclear or multinuclear, but uninuclear complexes are also formed, for example, with iron.[1,2,8] The largest increases in $\Delta[H]/[M]$ are associated with chelate formation:

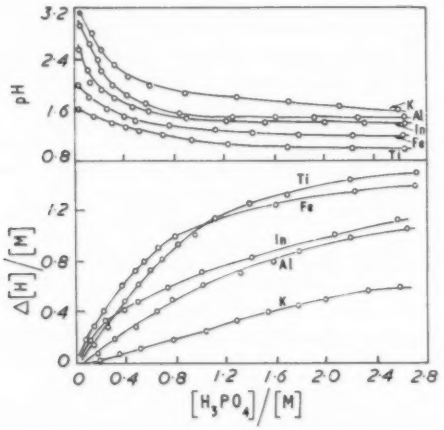
$$M^{3+} + H_3PO_4 \rightleftharpoons MHPO_4^+ + 2H^+ \ (H^+:M = 2:1)$$

rather than the formation of multinuclear ions by bridging:

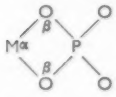
$$2M^{3+} + H_3PO_4 \rightleftharpoons M_2PO_4^{3+} + 3H^+ \ (H^+:M = 3:2)$$

Thus the very large increases in [H] obtained with iron and titanium probably reflect the greater tendency on the part of these metals to form chelate complexes.

FIG. 2.



The chelate complexes (inset) are formed essentially as four-membered rings and the tendency to form such complexes will be related to their stability. This, in turn, will be related to the size of the metal ion. If the size of the metal ion is such that the ring can be formed under strain-free conditions there will be every incentive for chelate rings to be formed and the resulting complex ion will show the maximum enhancement of stability owing to the "chelate effect." But if the metal ion is too large or too small, bridge structures will tend to be more stable. In the extreme case, very large cross-linked structures may be formed, leading to precipitation.



From the results, it appears that the ideal size is approximately 0·70 Å and that this is the explanation of the maximum complexing obtained with titanium and the lower values with other metals having ionic radii on either side of this. The metals considered in this work are all probably forming complexes by use of the outer *d* orbitals, that is, by sp^3d^2 hybridisation, and, although the general arguments used would still be true, it is not considered safe to extend the argument to the case of metals using inner *d* orbitals, particularly where ligands other than phosphate and aquo-groups may be involved.

It may be observed that whilst trischelate complexes are formed by aluminium, iron,[9a,b] and indium,[9d] monochelate structures are formed by iron [3,8] and, by inference from the present studies, titanium, but not apparently to any significant extent by alumimium or indium.[8c,d] The greater stability of the trischelate structures thus makes possible their formation over a wide range of ionic radii.

It is possible, with simple theoretical considerations, to calculate the optimum ionic radius for a strain-free ring. Using Pauling's values [10] for the ionic radii of O^{2-} and P^{5+} (1·40 and 0·34 Å) respectively, and assuming that the four oxygen atoms are grouped about the phosphorus atom tetrahedrally (O–P–O bond angle = 109°), we find the O–O distance to be 2·83 Å, showing that the oxygen atoms are roughly touching each other. It is not possible to reduce the phosphorus bond angle and equally it is not possible to keep both oxygen and metal bond angles (α and β) at 90°. If the strain is distributed between the two oxygen bond angles and the metal bond angles so that α is 84° and β is 83·5°, the M–O distance is 2·12 Å and the metal radius must be 0·72 Å.

Several factors suggested the use of ionic rather than covalent radii. Thus the interaction is between M^{3+} and effectively HPO_4^{2-} and will involve bonds of a highly polar character. Hence the oxygen atoms in P–O–M will carry effectively one unit of negative charge which may be increased further by the polar character of the P–O bond (about 40% for a single bond according to Pauling [11]). Further, the bonding of the two oxygen atoms to two other atoms (M and P) will reduce effectively the double-bonding between the phosphorus and the oxygen atom so that the bonds will be restored to 1·74 Å as compared with the commonly encountered 1·55 Å.[12] In addition the general similarities observed between the crystal structures of several heavy-metal phosphates and certain silicates [13] suggests that in these phosphates the structure is approximately one of large contiguous O^{2-} ions with smaller interstitial P^{5+} ions.

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[10] Pauling, "The Nature of the Chemical Bond," 2nd Edn., Cornell Univ. Press, 1940, p. 346.
[11] Pauling, *op. cit.*, p. 70.
[12] Van Wazer, *J. Amer. Chem. Soc.*, 1956, **78**, 5709.
[13] Wells, "Structural Inorganic Chemistry," 2nd Edn., Oxford Univ. Press, 1950, p. 488.

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284. *Spectra of Protactinium-(IV) and -(V) in Hydrochloric Acid.*

By D. BROWN, A. J. SMITH, and R. G. WILKINS.

Spectral changes occurring when protactinium(V) is reduced by zinc amalgam are noted.

As a preliminary to proposed studies of electron transfer between protactinium-(IV) and -(V), it was necessary to investigate the reduction of the latter in acid solution. Haissinsky and Bouissières [1] first obtained a reduced form of protactinium in acid solution by treating protactinium(V) with reducing agents, particularly zinc amalgam, and from co-precipitation experiments suggested it was protactinium(IV). Later they [2] investigated the behaviour of the reduced state towards various reagents (its most striking and distinguishing feature being the insolubility of the fluoride) and from oxidations with cerium(IV) confirmed that the reduced form was protactinium(IV). The most recent investigation [3] of protactinium(IV) in solution has been concerned with its solvent-extraction behaviour and, in particular, it was shown that Pa^{IV}, unlike Pa^{V}, was not extracted into isobutyl methyl ketone from 6M-hydrochloric acid.

Several solid protactinium(IV) compounds have been prepared [4] and the spectrum of a

[1] Haissinsky and Bouissières, *Compt. rend.*, 1948, **226**, 573; *J.*, 1949, S256.
[2] Haissinsky and Bouissières, *Bull. Soc. chim. France*, 1951, 146.
[3] Haissinsky and Bouissières, *Compt. rend.*, 1957, **244**, 573.
[4] Sellers, Fried, Elson, and Zachariasen, *J. Amer. Chem. Soc.*, 1954, **76**, 5935.

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solution from solid protactinium tetrachloride (in 1M-hydrochloric acid) has been examined.[5] We now report the conditions for complete zinc amalgam reduction of Pa^V, and the spectrum of the product, so as to compare it with that obtained by direct methods.[5] Preliminary experiments on the spectra of reduced protactinium in sulphuric and perchloric acids have been reported.[6]

Experimental

Materials.—The naturally-occurring α-active ^{231}Pa was used. The concentration of protactinium was determined by radio-assay in an argon gas-flow proportional counter, and the samples were mounted on tantalum trays. Protactinium was purified from its daughter elements before a set of experiments by extraction of Pa from 7M-hydrochloric acid by di-isopropyl ketone [7] followed by stripping into 6M-hydrochloric acid containing 0·2M-hydrofluoric acid. The radiochemical purity of the product was confirmed as $\geqslant 99\%$ by α-pulse analysis. Protactinium was further purified from other elements present such as niobium, aluminium, and iron, indicated by spectrography. The addition of anhydrous aluminium chloride to the HCl–HF solution allowed the extraction of protactinium into 0·5M-thenoyltrifluoroacetone in benzene. More than 85% of Pa was thus extracted and re-stripped into 6M-hydrochloric–0·2M-hydrofluoric acid solution. After addition of more aluminium chloride, the protactinium was re-extracted into fresh thenoyltrifluoroacetone in benzene, and after repeated washing of this extract with 6M-hydrochloric acid, was stripped into 0·2M-oxalic acid solution and precipitated by the addition of ammonia. The precipitate was quickly dissolved in cold concentrated hydrochloric acid to form the stock solution for the experiments. The second extraction with thenoyltrifluoroacetone ensures the complete elimination of iron(III) as shown by the absence of an absorption band around 360 mμ. Spectroscopic analysis of the final product showed the absence of other elements likely to interfere in the spectral study. Polythene apparatus was used in this work.

Thenoyltrifluoroacetone was distilled twice *in vacuo* before use, and di-isopropyl ketone distilled once. The other materials used were "AnalaR," where possible.

Reduction and Spectral Experiments.—The spectrum of protactinium(V) was examined in different molarities of hydrochloric acid, by dilution of the stock solution, shortly after it had been prepared as described above. All spectra were measured on a Unicam S.P. 500 spectrophotometer. Freshly prepared zinc amalgam (from "AnalaR" zinc shot) was used for reduction, which was carried out in an atmosphere of argon. At the end the protactinium solution was run into a spectrophotometer cell in an argon atmosphere and the cell was stoppered without exposure of the solution to the air. The effectiveness with which oxygen was excluded during these operations was confirmed by preparing 10^{-3}M-chromium(II) in the apparatus and noting the absence of absorption by chromium(III) from the final solution. For the measurement of spectra of protactinium(IV), a "blank" was prepared. Although there is strong absorption by mercury chloride complexes below 250 mμ, there are only small differences in absorption between two identically run blanks and from this, and the appearance of the final protactinium(IV) spectra, we conclude that the error introduced by the production of optically absorbing complexes during the reduction is small. All manipulations with protactinium were performed in a fume-cupboard and stringent precautions taken to avoid the spread of contamination.

Results and Discussion

The spectra of protactinium(V) in hydrochloric acid of different molarities are reproduced in Fig. 1. The work was almost completed before we learnt from Dr. A. G. Maddock that this system had been studied in more detail at the University Chemical Laboratories, Cambridge.[8] Where our results overlap, in general good agreement is found. In hydrochloric acid above 6M, one absorption band only is obtained (213 mμ) and although there are semblances of bands at around 260 mμ and 300 mμ these only develop at lower acidities.

[5] Fried and Hindman, *J. Amer. Chem. Soc.*, 1954, **76**, 4863.
[6] Elson, "The Chemistry of Protactinium," in "The Actinide Elements," edited by Seaborg and Katz (National Nuclear Energy Series), McGraw-Hill, New York, 1954, p. 125.
[7] Golden and Maddock, *J. Inorg. Nuclear Chem.*, 1956, **2**, 46.
[8] Casey and Maddock, *ibid.*, to be published.

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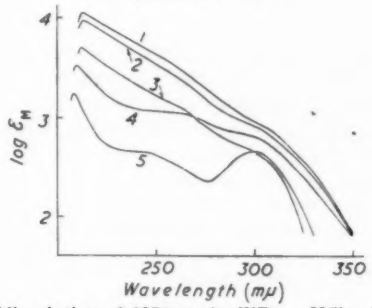
In 1·7M-hydrochloric acid there is a definite peak at 300 mμ, although in some solutions (at this acidity), because of the onset of hydrolysis and the appearance of a peak at 262 mμ, it appears only as a flattening and is not as pronounced as shown in Fig. 1. Like Casey and Maddock [8] we observe considerable spectral changes with time; for example, the peak at 300 mμ in 1·7M-hydrochloric acid disappears within a few hours and a strong peak at 262 mμ develops. The latter has been noted as characteristic of protactinium(V) in all acidities and is associated with the onset of hydrolysis which is accompanied by the disappearance of solvent extractability.[8]

The spectra of the products from the reduction experiments are shown in Fig. 2. The intense absorption band of protactinium(V) at 213 mμ is of great assistance in determining the conditions for complete reduction. We have always obtained incomplete reduction (curve 2) even with six hours' reduction if we commence with 4M-hydrochloric acid solutions. Provided, however, that the solution is at least 6M in hydrochloric acid at the commencement of reduction (it will finish at about 2M) then 5—6 hours is sufficient to complete the reduction of 10^{-4}M-protactinium(V) solutions (curve 1). We ascribe the incomplete reduction of protactinium at lower starting acidities to the presence of colloidal protactinium,[9] which defies easy reduction. The spectrum of protactinium(IV) shows lower optical absorption than protactinium(V), with the development of peaks at 229, 260, and 282 mμ with ε_M values of 470, 1010, and 1730 respectively. The general form of the absorption spectrum resembled closely that obtained by Fried and Hindman [5] by the dissolution of protactinium tetrachloride in M-hydrochloric acid, who report absorption (ε_M) and peak values of 425 (224 mμ), 980 (255 mμ), and 1520 (276 mμ). In fact the absorption curve is modified surprisingly little when it is remembered that our solutions are 1·7M in H^+ and 7M in Cl^-. In other experiments we find that the protactinium(IV) peaks are little affected in height or position by acidity changes from 1 to 3M at 6M-chloride-ion concentration.

When the solutions stand in air for about 1 hr., the three protactinium(IV) peaks

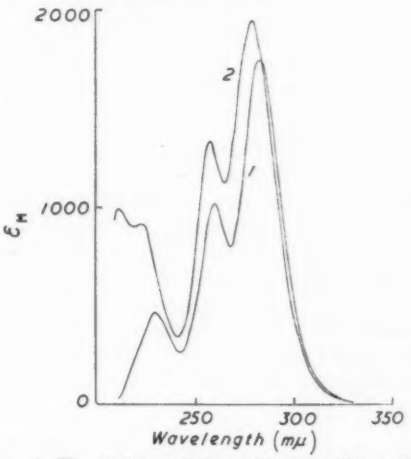
[9] Maddock and Miles, *J.*, 1949, S248.

FIG. 1. *Absorption spectra of protactinium(V) in hydrochloric acid.*



All solutions 0·0375mM in ^{231}Pa. HCl: 1, 11·1M; 2, 8·40M; 3, 5·83M; 4, 3·45M; 5, 1·7M.

FIG. 2. *Absorption spectra of protactinium(IV) in hydrochloric acid.*



1. Pa^{IV}: 0·133mM-^{231}Pa with 1·7M-H^+ and 7M-Cl^-. Initially Pa^V in 7M-HCl; reduction period 6 hr. 2. Pa^V–Pa^{IV} mixture, 0·178mM in ^{231}Pa, with 1·6M-H^+ and 4M-Cl^-. Initially Pa^V in 4M-HCl; reduction period 6 hr.

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disappear. The new spectra are not very reproducible and change with time as might be expected from the behaviour of the original protactinium(v). However the dominance of the 213 mμ peak has disappeared in the reoxidised solution and peaks at 213 mμ and 230 mμ are obtained which slowly become one peak at 230 mμ. We propose to examine the spectra of protactinium(v) and the reduced product in other acids.

We thank Mr. H. A. C. McKay, Dr. L. E. J. Roberts, and others at the Atomic Energy Research Establishment, Harwell, for help, the Authority for a grant and maintenance grant (to D. B.), and Dr. A. G. Maddock for information.

SHEFFIELD UNIVERSITY. [*Received, December 2nd,* 1958.]

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285. *Dynamic Contact Angles. Part II.*[1] *Air–Solution–Solid Contact Angles in Aqueous Solutions of Decyl Alcohol and Decanoic Acid.*

By T. A. ELLIOTT and L. LEESE.

Dynamic contact angles have been measured at the air–solution–paraffin wax interface for aqueous solutions of decyl alcohol and decanoic acid. The effects of changes in surface area are considered, and methods of calculating the air–liquid interfacial tensions discussed.

THAT the rates of change of contact angle for an air bubble on paraffin wax immersed in an aqueous solution of a normal alcohol (C_5—C_9) vary with the chain length and concentration of the solute [1] was attributed to differences in adsorption and desorption rates of the solutes. Dynamic contact angles for both equilibrium and non-equilibrium bubbles have been measured over a range of concentrations of decyl alcohol and decanoic acid.[2,3] Rapid changes in area of the air–solution interface of these solutes, which have long adsorption and desorption times, change the surface tension. During bubble contact, changes in area of the liquid–air interface occur, and ought to affect the surface tension and the contact angle. An attempt to determine the surface tension at the air–solution interface has been made, and the effect of changes in surface area considered.

EXPERIMENTAL

Apparatus.—The apparatus and procedure were as described in Part I.

Purification of Materials.—Decyl alcohol and decanoic acid (B.D.H.) were fractionally distilled under vacuum, and had, respectively, d_4^{20} 0·8289, —; b. p. 231·2°, 135°/4 mm.; m. p. —, 30·5°; n_D^{30} 1·4371, —. The surface tensions measured by the vertical-plate technique for decanoic acid solutions were lower than Addison's drop-weight results.[4] Addison and Hutchinson observed similar deviations for decyl alcohol solutions and concluded that the results obtained by the vertical-plate method were true static surface tensions.[5]

DISCUSSION AND RESULTS

In Figs. 1 and 2 are shown typical curves for both " equilibrium " (Curves *A*, *D*, *F*, *I* and *O*, *P*, *T*) and " non-equilibrium " (Curves *H*, *L*, *M* and *S*, *X*) bubbles.

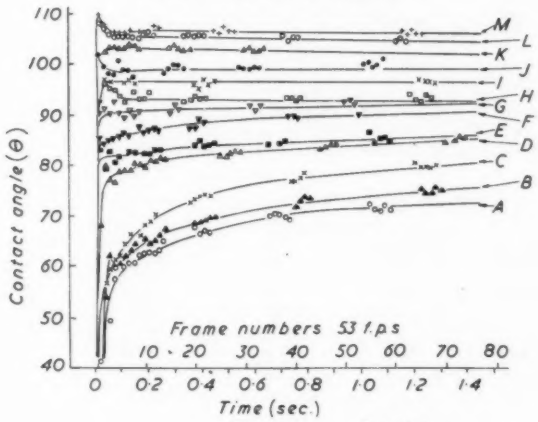
(a) *Induction Times.*—These were longer for bubbles with appreciable amounts of adsorbed solute, which is in accord with the suggestion that the disjoining film is stabilised by adsorption of solute.[6]

[1] Part I, *J.*, 1957, 22.
[2] Addison and Hutchinson, *J.*, 1949, 3404, 3406.
[3] Addison, Bagot, and McCauley, *J.*, 1948, 936.
[4] Addison, *J.*, 1946, 579.
[5] Addison and Hutchinson, *J.*, 1949, 3390.
[6] Bikermann, " Foams," Reinhold, New York, 1st Edn., 1953, pp. 162—169.

(b) *Contact-angle–Time Curves.*—The curves differed in several respects from those for the C_2—C_9 normal alcohol solutions: (i) The initial increase in angle for " equilibrium bubbles " was more rapid than would be expected from comparison with the octyl and nonyl alcohol solutions; (ii) the expected increase in the " long-term " effect was not observed; (iii) differences between " equilibrium " and " non-equilibrium " bubbles were very marked (cf. Curves *D* and *L*; *T* and *X*).

Effect (i) is more apparent in Fig. 3, where, for " equilibrium bubbles " in a range of C_5—C_{10} alcohol solutions ($\gamma = 50$ dynes/cm.), values of θ_t/θ_{te} are plotted against time;

FIG. 1. *Decyl alcohol solutions.*



Curve	Concn. (%)	γ (dynes/cm.)	Time on jet (sec.)	$\theta_r \pm 0{\cdot}5$ or $\theta_e \pm 0{\cdot}5$	$\theta + 0{\cdot}5$	Induction time (frames)
A	0·0024	39·8	60	73·3	80·1	10
B *	0·00127	50·0	60	87·8	89·5	4
C *	"	"	60	"	"	5
D	"	"	60	"	"	4
E	"	"	10	"	"	5
F	0·000819	56·4	60	91·2	94·2	7
G	"	"	10	"	"	12
H	0·00167	45·9	0	88·6	81·3	2
I	0·00055	61·4	60	97·5	99·0	13
J	"	"	20	102·7	102·7	2
K	"	"	10	99·3	100·1	5
L	0·00123	50·4	0	95·0	90·5	3
M	0·00055	61·4	0	104·6	101·7	1

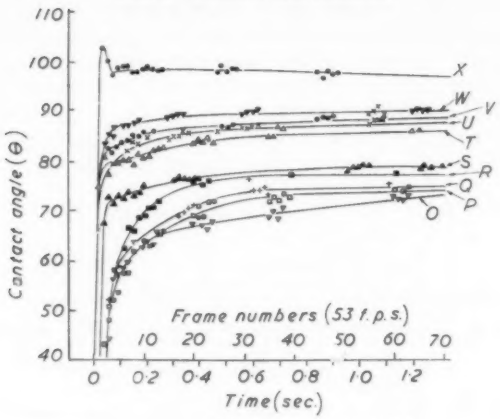
* Slow ejection technique.

θ_{rt} is the contact angle at time t and θ_{re} is the angle when the bubble has reached equilibrium.

Effects (i) and (ii) suggested that the bubbles were not carrying the equilibrium surface excess of solute owing to their ejection before adsorption of this excess was complete, and/or to their expansion during ejection. The effect of reducing the initial surface excess by reducing the adsorption time, while the bubbles were standing on the orifice, is shown by curves *I*, *J*, *K*, *M* of Fig. 1 and *T*, *U*, *V*, *X* of Fig. 2. Adsorption of solute during the passage of the bubble through the solution (less than 0·2 sec.) would be too slow to compensate for the decrease in surface excess caused by surface expansion.

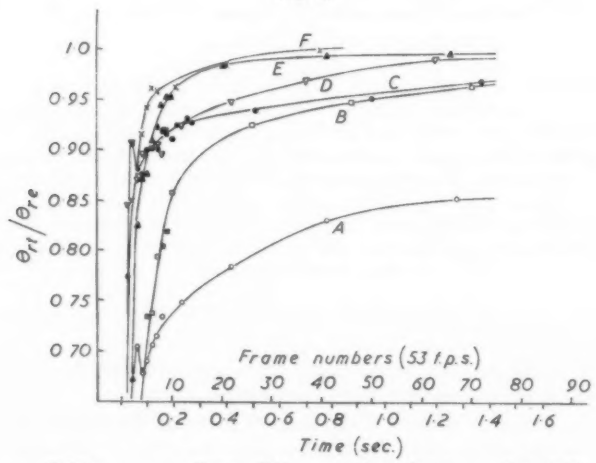
Both factors were minimised by slowly expanding the bubble almost to its maximum stable size and keeping it on the orifice for 1 min. before ejection; contact-angle–time

FIG. 2. *Decanoic acid solutions.*



Curve	Concn. (%)	γ (dynes/cm.)	Time on jet (sec.)	$\theta_r \pm 0{\cdot}5$ or $\theta_e \pm 0{\cdot}5$	$\theta_e \pm 0{\cdot}5$	Induction time (frames)
O	0·00414	38·6	60	75·5	80·9	27
P	0·00295	43·2	60	82·5	86·9	31
Q	"	"	10	83·0	86·5	32
R	"	"	20	84·1	87·4	21
S	0·00414	38·6	0	78·4	80·6	11
T	0·00170	51·2	60	88·4	90·9	3
U	"	"	20	89·6	90·8	2
V	"	"	10	89·3	89·6	3
W	0·00141	53·9	15	90·9	90·1	16
X	0·00170	51·2	0	98·6	92·8	1

FIG. 3.



Curve	Solute	Concn. (%)	γ (dynes/cm.)	$\theta_r \pm 0{\cdot}5°$	$\theta_e \pm 0{\cdot}5°$
A *	Decyl alcohol	0·00127	50·0	87·8	89·5
B	Nonyl alcohol	0·00426	50·6	84·9	87·5
C	Decyl alcohol	0·00123	50·4	87·8	89·4
D	Decanoic acid	0·00170	51·2	89·6	90·8
E	Heptyl alcohol	0·049	49·9	84·6	86·2
F	*n*-Pentyl alcohol	0·408	50·5	86·5	87·4

* The bubble was ejected slowly.

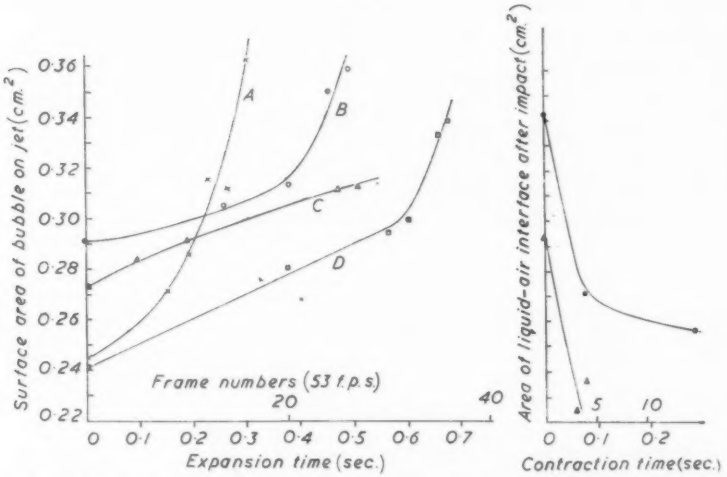
curves *B* and *C* of Fig. 1 (cf. Curves *D*, *E*, and *L*) were so obtained. Different rates of final ejection probably caused the discrepancy between curves *B* and *C*.

Surface expansion. Values of the surface expansion during bubble ejection were calculated from photographs of the ejection process and by the use of Guldinus's theorem.[3] Surface areas, plotted against time in Fig. 4, were used to calculate changes in Γ_{LA}, the surface excess, with time for solutions of decyl alcohol, as described below.

During ejection the surface excess is decreased by surface expansion, but is increased by contraction of the surface of the bubble when it is on the block. The calculations were extended to determine this effect (Fig. 5).

Calculation of Γ_{LA}. (*a*) Values of Γ_{LA} during bubble expansion were obtained from the experimental γ–concentration curve. It was assumed that the Gibbs adsorption

FIG. 4.



Curves *A*, *B*, *C*, slow ejection technique; Curve *D*, normal ejection technique.

equation applied for a dynamic system. The small adsorption to the surface during the expansion time (0·5 sec.) was neglected. (*b*) Values of Γ_{LA} after bubble contact were calculated (desorption during contraction being neglected) by use of three assumptions: (1) That all the solute adsorbed at the air–liquid interface remained there during contraction [Points (1), Fig. 5]; (2) that transfer of solute from the solid interface to the bubble surface occurred but only when the triple interface was outside the periphery of the circle of contact during the induction period, and that the acquired solute was uniformly distributed over the air–liquid interface [Points (2), Fig. 5]; (3) that solute was not lost from the liquid–air interface [Points (3), Fig. 5], and that solute transfer occurred from the entire solid–liquid interface covered by the bubble.

In order to apply assumptions (2) and (3), Γ_{LS} was calculated.

Calculation of Γ_{LS}. If Young's [7] equation $\gamma_{SA} + \gamma_{LA} \cos\theta = \gamma_{LS}$ applies to the system, then γ_{LS} can be calculated and hence Γ_{LS}, provided γ_{SA} and $\gamma_{LA} \cos\theta$ are known.

Fox and Zisman [8] reported that adsorption at the air–solid interface of a low-energy solid does not affect the surface energy. If γ_{SA} remains effectively constant over a range of concentrations, then a graph of $\gamma_{LA} \cos\theta$ against solute concentration will have the same shape as the plot of γ_{LS} against concentration. Hence the surface excess Γ_{LS} can be calculated by use of the Gibbs equation.

[7] Young, *Phil. Trans.*, 1805, **95**, 65.
[8] Fox and Zisman, *J. Colloid Sci.*, 1950, **5**, 514.

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The Γ_{LS}–concentration curve (Fig. 6, *B*) was calculated by use of values of $\gamma_{LA,e}$ corrected for the " bag effect " reported by Addison, Bagot, and McCauley,[3] by comparison with the γ_{LA}–θ_e curve for the shorter-chain alcohols.

Values of Γ_{LA} calculated from assumptions (1) [Points (1), Fig. 5] are smaller than the equilibrium values, although " equilibrium " bubbles would be expected to have at least the equilibrium surface excess. Assumptions (2) and (3) both give values higher than the equilibrium surface excess, but the values from assumption (2) [Points (2), Fig. 5] are in closest agreement with the true equilibrium value.

The initial fall in surface excess (Fig. 5) due to expansion of the surface of the bubble on

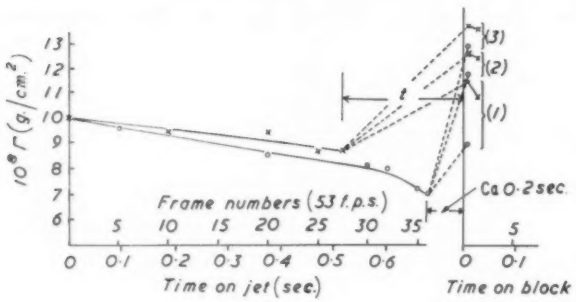


FIG. 5.

Curves *A* and *B* were derived from curves *C* and *D* (Fig. 4) respectively. The time-lapse *t* is about 0·2 sec.

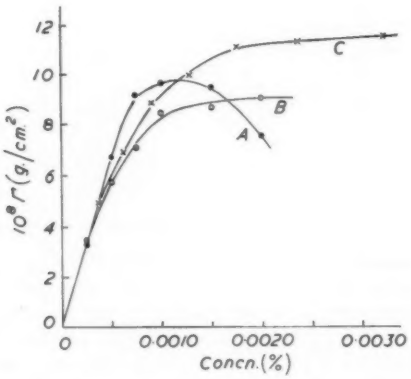


FIG. 6.

Curve *A* Γ_{LS} (calculated), *B* Γ_{LS} (corrected), *C* Γ_{LA} (calculated).

ejection is outweighed by the contraction of the surface on impact with the block. These opposing effects mutually compensate to give approximately the equilibrium surface excess on the block, and hence reduced the long-term effect which, for the shorter-chain alcohols, was attributed to the desorption of excess of solute into the bulk solution.

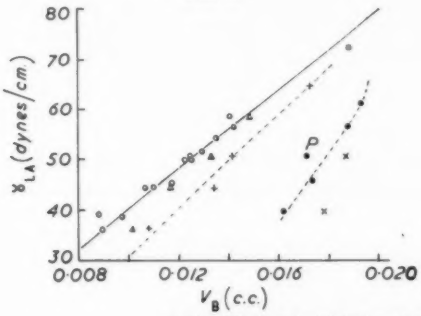
The values of γ_{LA} so obtained are given in Table 1, column (iii), for comparison with values obtained by other methods. The actual values of γ_{LA} corresponding to the calculated γ_{LA} should probably be several dynes/cm. higher to account for disorientation of the solute molecules.[2]

Determination of γ_{LA}.—*From the bubble volume.* In order to calculate the change in surface tension of the bubble on the block with time, it is necessary to know the surface tension at some instant. γ_{LA} on impact can be calculated from the volume of the bubble on the block, by equating this to the volume on ejection and using the normal drop-volume method, adsorption and changes in volume due to pressure change being neglected.

The full line in Figs. 7 and 8 represent bubble volumes on the orifice (*d* 0·101 cm.)

calculated from Harkins and Brown's tables.[9] The points represent experimental bubble volumes estimated (i) by calculation from observed heights and diameters of bubbles at equilibrium on the wax, the bubble being assumed to be a spherical cap with the measured contact angle, or (ii) by measurement of the dimensions of bubbles at equilibrium, and application of Guldinus's theorem. The scale factor (which is cubed in the calculation) is a source of error.

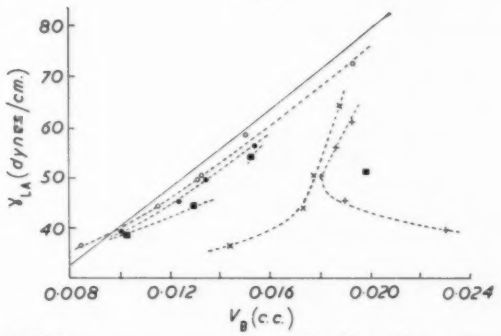
FIG. 7.



n-Alcohols	"Equilibrium bubble" volumes by (i) Calculation	(ii) Guldinus's theorem
C_2—C_5	○	
C_7	○	△
C_9	+	
C_{10}	●	×

P, C_{10} alcohol solution, $\gamma = 50$ dynes/cm.; slow ejection. The full line was derived from Harkins and Brown's tables.

FIG. 8.



Solute: normal alcohol	C_2—C_5	C_7	C_8	C_9	C_{10}
Non-equilm. bubble vol. by calcn.	○	●	■	×	+

The full line was derived from Harkins and Brown's tables.

In Fig. 7 agreement is good between calculated values [method (i)] and results obtained by use of Harkins and Brown's tables for solutions of C_5—C_9 alcohols. Slightly larger volumes were obtained by method (ii). The calculated bubble volumes give a value of surface tension of the solution within 10% of the true value. The increase in bubble volume for solutions of long-chain solutes, and comparable surface tensions, is a measure of the increase in the dynamic surface tension during the rapid expansion of the air–liquid interface on bubble ejection (Table 1).

[9] Harkins and Brown, *J. Amer. Chem. Soc.*, 1919, **41**, 499.

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"Non-equilibrium bubbles" showed an increase in dynamic surface tension for solutions of *n*-pentyl alcohol; the effect increased with the chain length of the solute. The high bubble volumes recorded for decyl alcohol solutions may be due to excess of air

TABLE 1. *Values of γ_{LA} (dynes/cm.) on bubble impact for decyl alcohol solution.*

γ_{LA} (measured)	γ_{LA} (dynes/cm.) calc. from (i) Bashforth and Adams's tables, (ii) bubble volume V_B, (iii) surface areas.				
	Equilm. bubbles		Non-equilm. bubbles		
	(i)	(ii)	(i)	(ii)	(iii)
39·8	66·5	65	>75	>75	
45·9		69		73	
50·6		68		69	60·0 *
56·4		75		71	
61·4		77		74	
50·0	63	66			55·6 †

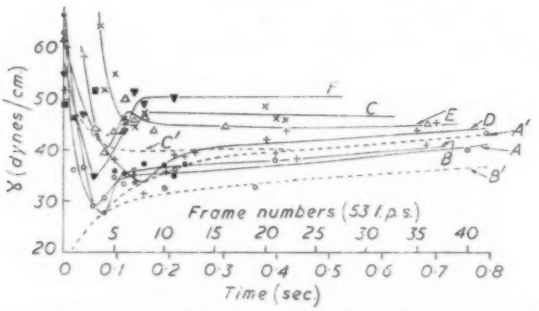
* "Equilibrium bubble." † Slow ejection technique.

Values * and † should probably be increased by about 8 dynes/cm. to account for the disorientation of the solute molecules.

flowing through the neck of the bubble, which is stabilised by adsorbed solute and collapses relatively slowly.

Use of Young's equation. If γ_{SA} and γ_{LS} are constant for a particular solution, then $\gamma_{SA} - \gamma_{LS} = \gamma_{LA,e} \cos \theta_e$ at equilibrium. Hence $\gamma_t = {}_{LA,e} \cos \theta_e / \cos \theta_t$. This equation fails when $\cos \theta_e$ and $\cos \theta_t$ have opposite signs, as θ_t passes through 90°.

FIG. 9.



Curve	Solute	γ (dynes/cm.)	Time on jet (sec.)	Ejection
A	Decyl alcohol	50	60	Slow
B	"	39·8	60	Equilm. bubble
C	"	39·8	0	Non-equilm. bubble
D	Decanoic acid	43·2	60	Equilm. bubble
E	"	43·2	0	Non-equilm. bubble
F	Ethyl alcohol	49·9	60	Equilm. bubble
			0	Non-equilm. bubble

A similar error occurs when γ_t is evaluated by comparison of θ_t with the appropriate curve of θ_e (receding) or θ_e (advancing) plotted against $\gamma_{LA,e}$. The use of the equilibrium curve assumes that the bulk concentration is such that γ_t is the equilibrium surface tension of the solution. The results so obtained (broken lines, Fig. 9) are slightly more reasonable than those obtained by the previous method.

Use of Bashforth and Adams's tables.[10] The dimensions of the bubbles were measured on enlarged photographs with a vernier microscope, and values of γ_{LA} (Points, Fig. 9) were calculated from the Tables. The full lines illustrate the trends only.

"Non-equilibrium" bubbles in decyl alcohol solution ($\gamma = 50$ dynes/cm.) gave

[10] Bashforth and Adams, "An Attempt to Test the Theories of Capillary Action," Cambridge, 1883.

unreasonably high results; the least was 66 dynes/cm. and the equilibrium contact angle gave a value of 76 dynes/cm.

An error of 1% in the contact angle would give rise to an error of 15—20% in the value of γ_{LA}. Calculations from the equilibrium bubble dimensions for solutions of higher concentrations also gave high values for γ_{LA}. It was concluded that Bashforth and Adams's treatment did not fully account for the shape of the bubble under the conditions of these experiments.

Interpretation of Results.—Short-term effect (0—5 *frames*). Peaks which always occur in the curves for " non-equilibrium " bubbles and frequently for " equilibrium bubbles," and extend over a maximum of four frames, are attributed to mechanical effects and not to changes in γ_{LA}.

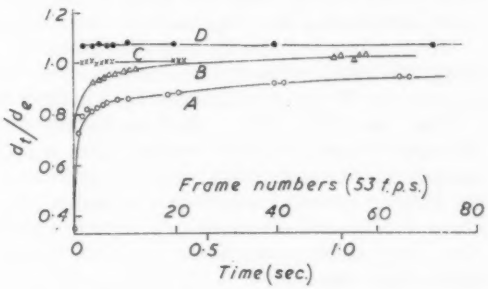


FIG. 10.

Curves *A* and *D*, $\gamma = 50$ dynes/cm.
B and *C* $\gamma = 40$ dynes/cm.

d_t base diameter at time t; d_e base diameter at equilm. before tapping.

The energy required to overcome viscous and frictional forces during spreading of the bubble will be due to gravitational and surface forces. If the buoyancy factor is neglected, the initial velocity of recession of the liquid will depend on $F = \gamma_{LA}(\cos\theta - \cos\theta_e)$, provided that Young's equation may be applied and $\gamma_{LS} - \gamma_{SA}$ remains constant during the recession. If the contact angle exceeds the equilibrium value, F becomes a restoring force and the contact angle should vibrate about the equilibrium. Small variations would be obscured by random errors in the measurement of contact angles. Peaks were not recorded for solutions of C_5—C_8 alcohols.[11]

Vibrations in the solutions of longer-chain solutes may be due to surface expansion on ejection, which causes γ_{LA} (on impact) to exceed $\gamma_{LA,e}$. γ_{LA}, which determines the velocity of recession, is continually reduced by contraction of the liquid–air interface and possibly by adsorption of solute from the solid–liquid interface. The moving liquid possesses too much kinetic energy to be damped out immediately by the viscous forces and the reduced restoring force when the equilibrium contact angle is reached. The liquid front therefore " overshoots " and the initial contact angle is increased.

For " non-equilibrium " bubbles, the diameter of the base remains practically constant during the succeeding rapid decrease in contact angle (Fig. 10, Curves *C* and *D*), which must be caused by a change in bubble shape.

For " equilibrium " bubbles, the base diameter continues to increase as the contact angle increases (Fig. 10, Curves *A* and *B*).

Rapid changes in contact angle (5—65 *frames*). Changes in contact angle depend on differences between the value of γ_{LA} at the moment of impact and its final equilibrium value. The initial value of γ_{LA} will depend on the time allowed for adsorption equilibrium before ejection, and on surface expansion of the bubble during ejection.

Long-term effect. The times for " non-equilibrium " bubbles to give constant contact angles are of the same order as the adsorption times (20—60 sec.) for decyl alcohol and decanoic acid solutions (15 sec.).

The final contact angles of equilibrium bubbles in decyl alcohol solutions are reached sooner than expected from desorption times. The lowest value of Γ_{LA} for slowly ejected

[11] Addison and Hutchinson, *J.*, 1949, 3396.

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bubbles (Fig. 5) corresponds to an initial value of $\gamma_{LA} = 45$ dynes/cm., comparable with an equilibrium value of 50 dynes/cm. Desorption of the excess of alcohol should require at least 200 sec. The equilibrium receding angle was reached after approximately 150 sec.

More rapid release of bubbles will involve greater rates of surface expansion and smaller initial values of Γ_{LA}; such bubbles should give static angles sooner, as confirmed.

Changes of contact angle above 90°. Results (Fig. 1) cannot be explained by changes in γ_{LA} alone. The rates of the short-term changes in contact angle are similar to rates of desorption from monolayers compressed below the normal surface area per molecule for a complete monolayer. Expansion of the bubble surface on ejection, and the slow adsorption rates of the solutes, cause the initial surface excess to be too low for a complete monolayer to be formed by compression of the liquid–air interface on bubble spreading.

Some solute is probably transferred from the solid–liquid to the liquid–air interface to bring the initial value of Γ_{LA}, for the normal equilibrium bubbles in solutions of decyl alcohol ($\gamma = 50$ dynes/cm.), below the equilibrium value.

For " non-equilibrium " bubbles the advancing contact angles which exceed 90° can be explained, provided it is assumed that γ_{LS} changes with time. It being assumed that the paraffin wax surface has been freed from solute molecules by the receding liquid, before the initial maximum contact angle is formed, the subsequent advance of the bulk liquid is across a clean solid–air interface to form a solid–liquid interface of high surface free energy. Hence the contact angle formed is equivalent to that where $\gamma_{LS} - \gamma_{SA}$ is larger than its equilibrium value.

Adsorption of solute to the clean solid–liquid interface governs the rate of change of the contact angle. (Below 90° the same mechanism will operate, but will be assisted by a fall in γ_{LA}.)

Analogous considerations apply to " equilibrium bubbles " with contact angle greater than 90°, where desorption from an overcrowded solid–liquid interface causes the slow increase in the angle.

It is considered that the contact angle formed by an air bubble at a solid–solution interface depends on the previous history of the bubble, as well as changes in interfacial tensions after impact with the solid.

We thank the City of Nottingham Education Committee for a grant (to L. L.).

NOTTINGHAM AND DISTRICT TECHNICAL COLLEGE. [*Received, July 10th,* 1958.]

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286. α-*Amino*-β-*keto-acids. Part I. Synthesis and Attempted Isolation of the Free Acids.*

By W. G. LAVER, A. NEUBERGER, and J. J. SCOTT.

α-Benzyl hydrogen α-amino-β-oxoadipate was prepared by selective transesterification of ethyl β-oxoadipate, nitrosation, reduction with stannous chloride, and hydrolysis of the δ-ethyl ester grouping. Benzyl α-amino-β-oxobutyrate hydrochloride was synthesized in an essentially similar manner. With both compounds catalytic hydrogenolysis occurred readily, but the speed of its decarboxylation rendered impossible the isolation of the α-amino-β-keto-acid formed. Similar instability of various α-acylamino-β-keto-acids was observed. Cleavage of the benzyl esters with hydrogen bromide in glacial acetic acid was slow and accompanied by decarboxylation. Attempts to isolate the desired free acids after reductive splitting of β-keto-α-phenylhydrazono-acids were also unsuccessful.

IT is now generally accepted that the first reaction in the biosynthesis of porphyrins consists of the condensation of succinyl-coenzyme A with glycine to give ultimately

δ-aminolævulic acid.[1 2 3] While the reaction can now be carried out *in vitro* with the aid of cell-free enzyme preparations,[4] certain features of the mechanism are still obscure; in particular it is uncertain at what stage the carboxyl group of glycine is lost. It is unlikely that glycine is decarboxylated before its condensation with succinate, since a variety of one-carbon compounds, such as methylamine, cannot be substituted for glycine.[5] However, the possibility that an activated complex of glycine loses carbon dioxide before condensation cannot be excluded. It is also possible that condensation takes place at the same time as the removal of the carboxyl group of glycine. The third possibility is that the primary product is α-amino-β-oxoadipate which is decarboxylated either by a specific enzyme or by spontaneous decomposition and this hypothesis was indeed preferred in the earlier publications.[1 2] In order to decide between some of these possibilities it was proposed to attempt the synthesis of α-amino-β-oxoadipic acid or at least to get information about the stability of this acid under physiological conditions.

No free α-amino-β-keto-acid has so far been prepared and attempts in this laboratory to hydrolyse ethyl and methyl α-amino-β-oxoadipate with acid or alkali without loss of carbon dioxide have been unsuccessful.[6] It seemed clear that α-amino-β-oxoadipic acid, if it existed at all, was not very stable. In the work to be reported in the present paper the α-benzyl ester of this acid was synthesized. It was hoped that hydrogenclysis of the ester would give the acid which could then be isolated under suitable conditions of temperature and pH. Ethyl β-oxoadipate with hot benzyl alcohol gave a benzyl ethyl ester to which structure (I) is ascribed. This is based on the fact that under the conditions used, *i.e.*, heating with the required alcohol without addition of a catalyst, transesterification occurs with esters of β-keto-acids, but not with esters of ordinary aliphatic acids.[7] Moreover, the structure proposed is the only one compatible with the reactions of the compound and the stability of the half-ester (III) derived from it which is described below. Nitrosation of the ester (I) by Adkins and Reeve's method [8] as modified by Albertson *et al.*[9] gave the crystalline α-hydroxyimino-compound (II). Reduction of the latter with stannous chloride in concentrated hydrochloric acid gave the monobenzyl ester (III) of the amino-keto-acid; the ester was isolated in the form of a crystalline toluene-*p*-sulphonate. The removal of tin salts resulting from the reduction of hydroxyimino-compounds by stannous chloride has generally been done by precipitation with hydrogen sulphide after the hydrochloric acid concentration has been lowered by addition of a large volume of water.[10] In the present work it was found that the stannic and stannous chloride can be completely and more conveniently removed by several extractions with ether. The salt of this half ester had m. p. 156·5—158° and did not lose carbon dioxide when heated; it is assumed therefore that the ester group in the β-position to the carbonyl group is still intact. The other ester group must have been split either during the reduction or during the subsequent working up in a strongly acid medium. The preferential hydrolysis of an ester group distal to the charged amino-group has been noted before in this group of compounds [6] and has been ascribed to the operation of electrostatic factors. Hydrogenolysis of the ester (III), with palladium as catalyst, under a variety of conditions yielded only δ-aminolævulic acid (IV). Quantitative aspects of this decarboxylation will be discussed in the following paper.[11]

[1] Shemin and Russell, *J. Amer. Chem. Soc.*, 1953, **75**, 4873.
[2] Neuberger and Scott, *Nature*, 1953, **172**, 1093.
[3] Shemin, Russell, and Abramsky, *J. Biol. Chem.*, 1955, **215**, 613.
[4] Laver, Neuberger, and Udenfriend, *Biochem. J.*, 1958, **70**, 4; Gibson, Laver, and Neuberger, *ibid.*, p. 71; Shemin, Kikuchi, and Bachmann, *Fed. Proc.*, 1958, **17**, 310; Kikuchi, Shemin, and Bachmann, *Biochim. Biophys. Acta*, 1958, **28**, 219; Gibson, *Biochim. Biophys. Acta*, 1958, **28**, 451.
[5] Unpublished experiments quoted by Shemin in "Ciba Foundation Symposium on Porphyrin Biosynthesis," J. and A. Churchill Ltd., London, 1955, p. 9.
[6] Neuberger, Scott, and Shuster, *Biochem. J.*, 1956, **64**, 137.
[7] Bader, Cummings, and Vogel, *J. Amer. Chem. Soc.*, 1951, **73**, 4195; see also Bacon, *Amer. Chem. J.*, 1905, **33**, 68.
[8] Adkins and Reeve, *J. Amer. Chem. Soc.*, 1938, **60**, 1328.
[9] Albertson, Tullar, King, Fishburn, and Archer, *ibid.*, 1948, **70**, 1150.
[10] Gabriel and Posner, *Ber.*, 1894, **27**, 1141.
[11] Laver, Neuberger, and Scott, following paper.

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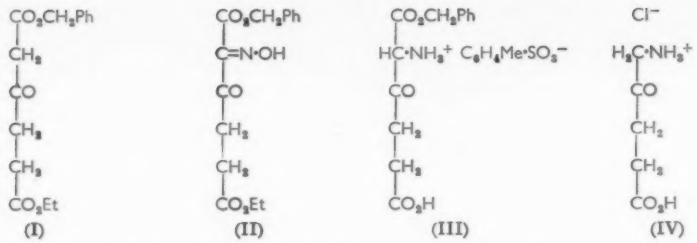

(I) (II) (III) (IV)

A similar series of reactions was carried out with benzyl acetoacetate. Nitrosation yielded a crystalline α-hydroxyimino-compound which on reduction with stannous chloride gave benzyl α-amino-β-oxobutyrate hydrochloride. After catalytic reduction aminoacetone but no α-amino-β-oxobutyric acid was isolated. In these catalytic reductions a palladium–charcoal catalyst was used in a strongly acid medium; under such conditions the hydroxyimino-group is readily reduced, but the carbonyl group is unaffected, as found by Harington and Randall.[12] However, with a platinum–palladium catalyst,[12] esters of α-amino-β-oxoadipic acid are reduced easily to derivatives of α-amino-β-hydroxyadipic acid which was isolated as a benzyloxycarbonylamino-compound. The material obtained was analytically pure, but probably consisted of a mixture of the two racemic forms as indicated by variations in m. p. of different crystalline fractions.

It seemed not impossible that the metal catalyst used in the catalytic hydrogenation might promote decarboxylation; other methods of preparing α-amino-β-oxoadipic acid were therefore explored. In the war-time penicillin work a crystalline α-hexanoylamino-β-oxopropionic acid was obtained which was unstable on storage.[13] It thus appeared likely that α-acylamino-β-keto-acids might be more stable than the α-amino-β-keto-acids themselves. Various monobenzyl esters of α-acylamino-β-oxoadipic acids and similar compounds in the acetoacetate series were therefore prepared in the hope that the esters might be hydrogenolysed without decarboxylation. The acylamino-linkage might then be split with the aid of enzymes such as amino-acid deacylases or by other methods. The acyl groups used were acetyl, chloroacetyl, benzyloxycarbonyl, and *p*-nitrobenzyloxycarbonyl. This approach was also unsuccessful, as the acylamino-keto-acids, although more stable than the amino-keto-acids, were too labile for isolation.

Similar negative results were obtained when the benzyl α-amino-β-oxo-adipate and -butyrate were treated with hydrogen bromide in glacial acetic acid at room temperature.[14] Liberation of benzyl bromide was slow and was accompanied by evolution of carbon dioxide. The *N*-benzyloxycarbonyl derivatives of the α-amino-β-keto-acids, unlike those of simple amino-acids,[14] were very slowly split by the hydrogen bromide reagent and decarboxylation was always associated with the removal of the acyl group.

Concurrently with these approaches, the reduction of β-oxo-α-phenylhydrazonobutyric acid and of the corresponding derivative of β-oxoadipic acid was explored. But again, apart from aniline, only aminoacetone or aminolævulic acid was obtained and the volume changes[11] occurring during the reduction indicated that decarboxylation under these conditions was even faster than during the hydrogenolysis of the benzyl esters described above. It seemed likely that the aniline formed during the reaction would promote decarboxylation, and the reduction of *N*-acetylphenylhydrazono-acids was therefore examined. But these attempts were also not successful. However, the use of *N*-acetyl derivatives which yield acetanilide on reductive fission[15] permits easy separation by ether-extraction of the two cleavage products of the reduction, as shown by the preparation of

[11] Harington and Randall, *Biochem. J.*, 1931, **25**, 1917.
[13] Cornforth, Cornforth, Abraham, Baker, Chain, and Robinson CPS. 59. Quoted by Cornforth in "The Chemistry of Penicillin," Princeton Univ. Press, 1949, p. 805.
[14] Ben-Ishai and Berger, *J. Org. Chem.*, 1952, **17**, 1565.
[15] Bülow and Hailer, *Ber.*, 1902, **35**, 915.

ethyl α-amino-β-oxobutyrate hydrochloride. The method is limited to preparation of the amino-keto-esters, as repeated attempts to isolate free α-*N*-acetylphenylhydrazono-β-oxobutyric acid failed owing to the readiness with which the compound reacted with the solvent to give the phenylhydrazono-acid. It is concluded that α-amino-β-keto-acids were indeed formed in the various reactions studied, but that they were too unstable to be isolated by conventional methods.

Experimental

Almost all evaporations were done under reduced pressure. Ultraviolet absorption data for many of the compounds mentioned here are given in the following paper.[11] Chromatography was done throughout on Whatman No. 1 paper with butan-1-ol–water–acetic acid (63 : 27 : 10, by vol.). Aminolævulic acid was identified by isolation as either the hydrochloride or the toluene-*p*-sulphonate and determination of mixed m. p. or by chromatography (R_F of the hydrochloride = 0·22 [16]); the compound was detected by spraying the paper either with butanolic ninhydrin (yellow colour after 2 min. at 80°) or with ammoniacal silver nitrate (reduction within 2 min., but not immediate as with α-amino-β-keto-esters [6]).

α-Benzyl δ-Ethyl β-Oxoadipate.—Ethyl β-oxoadipate (142 g.) was heated with benzyl alcohol (284 ml.) for 4½ hr. at 140°, a slow stream of nitrogen being passed through the mixture to remove the ethanol liberated. Distillation yielded *α-benzyl δ-ethyl β-oxoadipate* (144 g., 79%), b. p. 164—172°/0·8 mm., 152—160°/0·4 mm. (Found: C, 64·5; H, 6·6. $C_{15}H_{18}O_5$ requires C, 64·6; H, 6·45%).

α-Benzyl δ-Ethyl α-Hydroxyimino-β-oxoadipate.—To a solution of benzyl ethyl β-oxoadipate (144 g.) in glacial acetic acid (300 ml.) was added a solution of sodium nitrite (95% pure; 40·3 g.) in water (90 ml.) during 1 hr., at 25°. Water was then added, just insufficient to cause separation of two phases, and stirring was continued for 1½ hr. The mixture was then extracted with ether; the ether extract was washed free from acid with water and aqueous sodium hydrogen carbonate and dried. Removal of the solvent yielded the *oxime* which on crystallization from benzene–light petroleum (b. p. 40—60°) gave hexagonal plates (142 g., 89%). Recrystallization from chloroform–light petroleum (b. p. 40—60°) gave material of m. p. 72—74° (Found: C, 58·4; H, 5·4; N, 4·3. $C_{15}H_{17}O_6N$ requires C, 58·6; H, 5·6; N, 4·6%).

*α-Benzyl Hydrogen α-Amino-β-oxoadipate Toluene-*p*-sulphonate.*—α-Benzyl δ-ethyl α-hydroxyimino-β-oxoadipate (77 g.) was added during 7 hr. to a solution of stannous chloride dihydrate (125 g.) in hydrochloric acid (130 ml.; *d* 1·18). Ethanol (25 ml.) was added at the start of the reaction to facilitate dissolution of the oxime, and the temperature of the reaction mixture was kept below 28°. After all the oxime had dissolved, the solution was left at 20° for 15 hr. and then extracted with ether (4 × 600 ml.). The aqueous residue, on evaporation, gave a viscous oil which solidified to a glass on being dried *in vacuo* over sodium hydroxide but did not crystallize. This material was dissolved in the minimum amount of acetone, and a small amount of insoluble material was removed, consisting of small pyramidal crystals which charred, but did not melt, when heated. Ether was then added and an oil precipitated which again formed a solid glass after removal of the solvent and drying *in vacuo* over sodium hydroxide. Chromatography of this glass on paper showed one major ninhydrin-reacting spot (R_F 0·56) which almost certainly consisted of benzyl hydrogen α-amino-β-oxoadipate hydrochloride, but attempts to crystallize it at this stage failed.

The crude hydrochloride was dissolved in water (600 ml.), and Deacidite G (Permutit Co.) in the basic form (−16 + 50 mesh) was added with stirring until the pH rose to approx. 3·5. At this stage a gelatinous precipitate was formed which was removed together with the resin by rapid filtration. Toluene-*p*-sulphonic acid (43 g.) was added to the filtrate, which on concentration yielded crystalline *benzyl hydrogen α-amino-β-oxoadipate toluene-*p*-sulphonate* (35 g., 32% based on weight of oxime). Recrystallization from water gave rosettes, m. p. 155—157°, and from dry ethanol–ether needles, m. p. 156·5—158° (Found: C, 54·9; H, 5·5. $C_{13}H_{15}O_5N,C_7H_8O_3S$ requires C, 54·9; H, 5·3%). Paper chromatography gave a single spot of R_F 0·73 after spraying with 1% (w/v) butanolic ninhydrin or ammoniacal silver nitrate solution. The toluene-*p*-sulphonate was converted into the hydrochloride by passing an aqueous solution through a column of ion-exchange resin Deacidite FF (Permutit Co.) in the chloride form. The effluent was taken to dryness *in vacuo* over NaOH, and the residue of

[16] Berlin, Neuberger, and Scott, *Biochem. J.*, 1956, **64**, 80.

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α-benzyl hydrogen α-amino-β-oxoadipate hydrochloride crystallized from dry ethanol–ether as needles, m. p. 77—85°. Recrystallization from methanol–ether gave solvated needles, m. p. 82—85° (Found: C, 50·8; H, 6·25; N, 4·4; Cl, 10·6. $C_{13}H_{15}O_5N,HCl,CH_3{\cdot}OH$ requires C, 50·4; H, 6·0; N, 4·2; Cl, 10·6%). Catalytic hydrogenation with palladium–charcoal [12] was done under a great variety of conditions, *i.e.*, by varying the amount of catalyst or solvent or pH, but the only nitrogenous product obtained was aminolævulic acid (these experiments are described in the following paper [11]). The same result was obtained when the charcoal which was used as support for the catalyst was replaced by Celite 545 (Johns-Manville) which had been extensively washed with acid and then water, to remove metallic impurities.

The toluene-*p*-sulphonate of the benzyl ester (2·185 g., 5 mmoles) was dissolved in 50% (w/v) hydrogen bromide in glacial acetic acid (30 ml.) and kept at room temperature. Samples (5 ml.) were withdrawn at intervals, diluted with water (100 ml.), and extracted once with di-*n*-butyl ether (40 ml.). The ether layer was washed twice with water, once with saturated sodium hydrogen carbonate, and again twice with water. Ethanolic 0·1N-silver nitrate (10·0 ml.) was added, and the mixture was set aside for 10 min. Dilute nitric acid (5 ml.) and a few drops of ferric ammonium sulphate solution were then added, and the excess of silver nitrate was estimated by titration with aqueous 0·1N-ammonium thiocyanate. Results were as follows:

Time (min.)	3	25	120	300	1380	Theor.
CH_3PhBr liberated (mmole) ...	0·016	0·048	0·19	0·36	0·57	0·83

There was also evolution of carbon dioxide; this was not accurately measured, but the amount appeared to be smaller than expected on the basis of the benzyl bromide formed.

α-Benzyl Hydrogen α-Acetamido-β-oxoadipate.—To a suspension of the foregoing toluenesulphonate (4·37 g.) in glacial acetic acid (25 ml.) were added successively acetic anhydride (1·5 ml.) and anhydrous sodium acetate (0·82 g.). The mixture was shaken until complete solution was obtained and then left for 20 hr. at 20°. Dry ether (600 ml.) was added and the precipitate of sodium toluene-*p*-sulphonate was filtered off. The filtrate was concentrated to about 100 ml.; adding light petroleum (b. p. 40—60°) precipitated an oil which soon solidified. Recrystallization from hot water gave *benzyl hydrogen α-acetamido-β-oxoadipate* (2·41 g., 78%), m. p. 104—105·5°. Recrystallization from water gave plates (m. p. 105·5—106°), which on drying *in vacuo* over sodium hydroxide formed a powder (Found: C, 58·4; H, 5·6; N, 4·4. $C_{15}H_{17}O_6N$ requires C, 58·6; H, 5·6; N, 4·6%). Further recrystallization from water or from chloroform–light petroleum gave crystals which either softened at 105·5° and melted at 130—131·5° or melted at the higher temperature without preliminary softening. The differences in behaviour could not be correlated with the nature of the solvent used for crystallization. Moreover, it could be shown that the lower-melting form was not a hydrate.

Benzyl Hydrogen α-Chloroacetamido-β-oxoadipate.—To a suspension of benzyl hydrogen α-amino-β-oxoadipate toluene-*p*-sulphonate (6·22 g.) in glacial acetic acid (30 ml.) were added successively chloroacetic anhydride (2·55 g.) and anhydrous sodium acetate (1·168 g.). After 15 hr. ether was added and sodium toluenesulphonate removed. The filtrate was concentrated to about 100 ml. and light petroleum (b. p. 40—60°) was added. The resulting oil, which partially crystallized, was taken up in a large volume of hot water. On cooling, needles separated (1·33 g., 27·5%). Recrystallization from ethanol–water gave needles, m. p. 114—115° (Found: N, 4·1; Cl, 10·3. $C_{15}H_{16}O_6NCl$ requires N, 4·1; Cl, 10·4%).

Ethyl α-Hydroxyimino-β-oxoadipate.—Nitrosation of the ethyl β-oxoadipate was carried out as described above for the corresponding ethyl benzyl ester. After evaporation of the ether, the residue was heated for 2 hr. *in vacuo* on a boiling-water bath to remove traces of water. The product, a light brown oil, was left at −10° for a few weeks until crystallization occurred. The crude *ethyl α-hydroxyimino-β-oxoadipate*, recrystallized from cold (0°) toluene–light petroleum (b. p. 40—60°), gave rectangular needles, m. p. 53—55° (Found: C, 48·9; H, 6·2; N, 5·5. $C_{10}H_{15}O_6N$ requires C, 49·0; H, 6·2; N, 5·7%).

α-Benzyloxycarbonylamino-β-hydroxyadipic Acid.—Ethyl α-amino-β-oxoadipate hydrochloride (10 g.), dissolved in water (75 ml.), was reduced at atmospheric pressure in the presence of platinum–palladium–charcoal prepared as follows.[12] Palladium–charcoal (10 g.) was added to a mixture of platinum chloride (0·5 g.) and ferric chloride (0·025 g.) dissolved in water (10 ml.) containing two drops of concentrated hydrochloric acid; the suspension was then equilibrated with hydrogen. After addition of the ester, hydrogen uptake during 1½ hr. amounted to the

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theoretical. The catalyst was filtered off and the filtrate was concentrated to dryness. Ethyl α-amino-β-hydroxyadipate hydrochloride was obtained as a colourless syrup which partly crystallized after some time, but was not purified further. The hydroxy-ester was boiled in 2N-hydrochloric acid (200 ml.) under reflux for 2 hr. The product on evaporation yielded α-amino-β-hydroxyadipic acid as a glass which slowly crystallized but was not further purified. It was dissolved in N-sodium hydroxide (60 ml.) and left at 20° for 15 hr. The solution was then cooled to 0° and benzyl chloroformate (8 g.) was added. The mixture was shaken and N-sodium hydroxide (45 ml.) was added during 30 min., the pH being kept at about 9. The mixture was left for 1 hr. at 0° and then extracted three times with ether. The aqueous layer was acidified with hydrochloric acid until acid to Congo Red and then extracted several times with ethyl acetate. The ethyl acetate extracts were washed twice with water, dried (Na_2SO_4), and filtered. Concentration of the filtrate yielded *α-benzyloxycarbonylamino-β-hydroxyadipic acid* (4·5 g., 40%), m. p. 133—134° (Found: C, 53·8; H, 5·8; N, 4·1. $C_{14}H_{17}O_7N$ requires C, 54·0; H, 5·5; N, 4·5%). On recrystallization from acetone–light petroleum (b. p. 40—60°) the m. p. was 134—135°.

Addition of light petroleum (b. p. 40—60°) to the ethyl acetate liquor yielded crystalline material (m. p. 123—127°) which on recrystallization from ethyl acetate gave material of m. p. 137—138°.

Ethyl α-p-*Nitrobenzyloxycarbonylamino*-β-*oxoadipate*.—A mixture of ethyl α-amino-β-oxoadipate hydrochloride (6 g.) in water (60 ml.) with *p*-nitrobenzyl chloroformate [17] (6 g.) in ether (60 ml.) was cooled to 0°, and magnesium oxide (2·64 g.) was added in portions with intermittent shaking during 15 min. After a further 15 min. at 0°, the mixture was filtered and the ether layer was separated. The aqueous layer was acidified and extracted with ether. The ether extracts were pooled, washed with water and aqueous sodium hydrogen carbonate, dried, and evaporated. The residue on crystallization from cold (0—10°) ethanol–water yielded needles (7·6 g., 82%). On recrystallization from ethanol–water *ethyl* p-*nitrobenzyloxycarbonylamino*-β-*oxoadipate* had m. p. 52—55° (Found: C, 52·7; H, 5·4; N, 6·7. $C_{18}H_{22}O_9N_2$ requires C, 52·7; H, 5·4; N, 6·8%).

Benzyl α-p-*Nitrobenzyloxycarbonylamino*-β-*oxoadipate*.—Ethyl α-*p*-nitrobenzyloxycarbonylamino-β-oxoadipate (2·05 g.) was refluxed under a fractionating column with benzyl alcohol (6·6 g.), toluene-*p*-sulphonic acid (400 mg.), and benzene (60 ml.) for 12 hr. More toluenesulphonic acid (400 mg.), benzyl alcohol (6 g.), and benzene were then added and the mixture was refluxed for a further 1½ hr. Ethanol (270 mg.) was evolved during this period and collected in the distillate. The solution was then washed with water and dried and light petroleum (b. p. 80—100°) was added. An oil was precipitated which partly crystallized after some time at −10°. Filtration yielded a pasty residue which was dissolved in hot ether under pressure. On cooling, crystals formed. These were filtered off and recrystallized from ether (yield 520 mg., 20%). The *benzyl ester* had m. p. 82—84° (Found: C, 62·6; H, 5·1; N, 4·8. $C_{28}H_{26}O_9N_2$ requires C, 62·9; H, 4·9; N, 5·2%). Catalytic hydrogenation (palladium–charcoal [12]) of the ester gave aminolævulic acid. On treatment of the ester with a saturated solution of hydrogen bromide in glacial acetic acid there was a very slow evolution of carbon dioxide during several days. Working up these solutions under a variety of conditions yielded aminolævulic acid as the only identifiable aliphatic compound.

β-*Oxo*-α-*phenylhydrazonobutyric Acid*.—The ethyl ester [18] (2·34 g., 0·01 mole) was dissolved in ethanol (10 ml.), and 3N-sodium hydroxide (0·01 mole) was added (Bülow [19] used 3 equiv. of sodium hydroxide). The free acid was isolated essentially by Bülow's procedure. After recrystallization from hot chloroform–*cyclo*hexane, it had m. p. 161°, in agreement with Bülow. The yield was 96%. The benzyl ester (see below), treated similarly, gave needles, having m. p. 159°, raised to 161° after recrystallization.

Benzyl β-*Oxo*-α-*phenylhydrazonobutyrate*.—Aniline hydrochloride (51·8 g.; 0·4 mole) was dissolved in 3N-hydrochloric acid in a 2 l. flask. Throughout the subsequent diazotization the solution was slowly stirred mechanically and kept at 0—5° by external cooling. A solution of sodium nitrite (30 g.; 95% pure, in 80 ml. of water) was added during about 2 hr., until free nitrous acid persisted in the solution for 5 min. Benzyl acetoacetate (76·9 g., 0·4 mole) mixed with ethanol (500 ml.) was then added, followed at once by powdered sodium acetate (122·5 g.,

[17] Carpenter and Gish, *J. Amer. Chem. Soc.*, 1952, **74**, 3818.
[18] Kjellin, *Ber.*, 1897, **30**, 1965.
[19] Bülow, *Ber.*, 1899, **32**, 200.

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0·9 mole of the trihydrate). Cooling was stopped but stirring was continued at a greatly increased rate. After 15 min. most of the sodium acetate had dissolved; the colour of the solution was lemon-yellow. Shortly after the addition of water (100 ml.) spontaneous crystallization of the product yielded a thick paste. Rapid stirring was continued for 30 min.; the crystals were collected and washed with water (1 l.). After drying *in vacuo*, the crude material (m. p. 109—112°) weighed 115 g.; a further crop (2·5 g.) was obtained from the filtrate and washings after refiltration the next day (combined yield close to 100%). *Benzyl β-oxo-α-phenylhydrazonobutyrate* after recrystallization from hot aqueous ethanol had m. p. 98—100° (112 g.). A further crystallization from methanol gave material of m. p. 111·5—113·5° (Found: C, 68·7; H, 5·3. $C_{17}H_{16}O_3N_2$ requires C, 68·9; H, 5·5%). After further recrystallizations from *cyclo*hexane the m. p. were 102—106°, 76—78°, and 76—78° (Found: C, 69·1; H, 5·3%). The analytical samples of low and high m. p. had mixed m. p. 65—69°. When the low m. p. form was recrystallized from hot aqueous ethanol it had m. p. 109—111°. Both forms appeared as golden needles; both were convertible in 98% yield into 3-methyl-1-phenyl-4-phenylhydrazono-5-pyrazolone, whose m. p. (157—158°) was not depressed on admixture with a sample (m. p. 158—159°) prepared similarly from the ethyl ester, by the method of Japp and Klingemann;[20] Eibner[21] found m. p. 158°. Hydrogenation in a freshly prepared solution of hydrogen chloride (2 equiv.) in acetic acid gave aniline hydrochloride and aminoacetone hydrochloride (identified chromatographically).

Benzyl α-(N-Acetylphenylhydrazono)-β-oxobutyrate.—In contrast to the ethyl ester,[15] preparation of this compound was unsuccessful if an excess of acetic anhydride or an increased proportion of zinc chloride was present, or if heating was prolonged. After short periods of heating with an excess of reagents all the starting material was recovered unchanged; with longer periods of heating a dark brown tar was formed. Anhydrous zinc chloride (100 mg.) was dissolved in acetic acid (50 ml., dried by distillation over $CaSO_4$). Benzyl β-oxo-α-phenylhydrazonobutyrate (2·96 g.; m. p. 76—78°) was added, followed by acetic anhydride (1·02 ml.). The mixture was heated on a boiling-water bath for 1 hr., then rapidly cooled; water (10 ml.) was added slowly and crystallization was induced by scratching. The mixture was filtered, leaving nearly colourless crystals (2·0 g.; m. p. 126—130°); more water (150 ml.) was added to the filtrate, producing a further crop (1·27 g.; m. p. 120—125°). The crops were combined and recrystallized after dissolution in *cyclo*hexane (200 ml.) under reflux, yielding colourless needles (2·4 g., 71%) of the desired *N-acetyl ester*, m. p. 137° (Found: C, 67·5; H, 5·5; N, 8·0. $C_{19}H_{18}O_4N_2$ requires C, 67·4; H, 5·4; N, 8·3%). Yields were consistently 10—15% lower when the high-melting benzyl ester was used. The *N*-acetyl compound was hydrolysed rapidly by hot water, as judged by appearance of a yellow colour.

On catalytic reduction (palladium–charcoal [13]) in acetic acid not containing hydrogen chloride the benzyl group only was removed, yielding a colourless solution which rapidly became yellow in air during removal of the solvent, to give β-oxo-α-phenylhydrazonobutyric acid in quantitative yield. Hydrogenation in acetic acid containing 2 equivs. of hydrogen chloride yielded acetanilide, aniline hydrochloride, and aminoacetone hydrochloride.

Ethyl α-Amino-β-oxobutyrate Hydrochloride.—A suspension of palladized charcoal (3 g.) in a freshly prepared solution of dry hydrogen chloride (1·0 g.) in acetic acid (50 ml.) was equilibrated with hydrogen. A solution of ethyl α-(*N*-acetylphenylhydrazono)-β-oxobutyrate (2·76 g., 0·01 mole) in acetic acid (50 ml.) was then added and worked in with a further 50 ml. of acetic acid. Uptake of hydrogen (0·04 g.-atom) proceeded at a rate compatible with a single first-order reaction ($t_{\frac{1}{2}}$ 5·6 min.). After 1 hr. the catalyst was separated on a centrifuge, and the solvent by distillation, with exclusion of moisture. On extraction of the residue with warm dry ether (3 × 25 ml.) acetanilide (1·27 g., 94%) was removed and identified by m. p. and mixed m. p. (114—115°) after recrystallization from water. The material insoluble in ether crystallized after drying *in vacuo*; recrystallized from dry ethanol–ether it had m. p. 113·5—114·5° (decomp.), raised to 114—116° when mixed with the hydrochloride (m. p. 115—117°; decomp.) prepared by hydrogenation of the α-hydroxyimino-ester. Gabriel and Posner[10] gave m. p. 95° (decomp.). Potentiometric titration showed a $pK' = 5·2$; the equiv. wt. was 181 (calc. for $C_6H_{11}O_3N,HCl$: 181·6). The yield was 1·5 g. (83%).

Ethyl α-(N-Acetylphenylhydrazono)-β-oxoadipate.—Ethyl β-oxoadipate (20·4 g., 0·1 mole) in ethanol (125 ml.) was brought into reaction with benzenediazonium chloride (prepared on

[20] Japp and Klingemann, *Annalen*, 1888, **247**, 190.
[21] Eibner, *Ber.*, 1903, **36**, 2687.

one-quarter the scale described above) by addition of sodium acetate (47·6 g. of the trihydrate). Since the product was an oil, the mixture was transferred to a separatory funnel and extracted with benzene (3 × 150 ml.). The extracts were washed with water (5 × 100 ml.) and dried; benzene was removed by distillation. The yield of the crude phenylhydrazono-compound was theoretical. To this material was added a suspension of crushed anhydrous zinc chloride (1 g.) in acetic acid (100 ml.), followed by acetic anhydride (9·45 ml.). After 1 hour's heating on a boiling-water bath the product was crystallized and separated as described for the corresponding derivative of benzyl acetoacetate. Recrystallization was first from ethanol and then from *cyclo*hexane, giving material of m. p. 98—99° and 98·5—99·5° respectively. The pure *N-acetyl compound* (7·6 g., 23·7%) formed colourless octagonal plates (Found: C, 59·7; H, 6·1. $C_{16}H_{20}O_5N_2$ requires C, 60·0; H, 6·3%).

3-2′-Ethoxycarbonylethyl-1-phenyl-4-phenylhydrazono-5-pyrazolone.—By the procedure described [20] for preparation of the 3-methyl analogue of the foregoing pyrazolone, crude ethyl β-oxo-α-phenylhydrazonoadipate was cyclized with phenylhydrazine to the corresponding pyrazolone in 82% yield. The product recrystallized from hot benzene–ethanol. During subsequent cooling the orange-yellow needles (m. p. 115—117°) underwent a reversible allomorphic change, below about 40°, to orange rectangular plates. When these were heated in a Kofler apparatus, they lost their specific form between 40° and 60° (depending on the rate of heating) before melting at 115—117°. A similar change attended a further crystallization from *cyclo*hexane–ethanol, giving hexagonal plates of m. p. 117—118° after transition below 60° (Found: C, 65·9; H, 5·3; N, 15·3. $C_{20}H_{20}O_3N_4$ requires C, 65·9; H, 5·5; N, 15·4%).

Benzyl α-Hydroxyimino-β-oxobutyrate.—By using the proportions of reagents described below but otherwise following the procedure of Adkins and Reeve [8] for preparation of the corresponding ethyl ester, the desired product was obtained on the first occasion as a pale yellow oil which crystallized after keeping for a day at −10° (yield 90%). Subsequent preparations were simplified and the yield improved by seeding the reaction mixture. This modification is of no use in preparation of the ethyl ester, because crystals of the latter compound form an oil in the presence of water.

Benzyl acetoacetate (192 g., 1·0 mole) was mixed with acetic acid (200 ml.) in a cooled 2 l. flask. A solution of sodium nitrite (77·6 g., 95% pure) in water (160 ml.) was added slowly (about 1 drop/2 sec. during 1·5 hr.) with mechanical stirring so that the temperature was between 23° and 25° and the flask contents remained colourless. When most of the nitrite solution (150 ml.) had been added further addition caused development of a brown colour. A further portion (5 ml.) was added dropwise 15 min. later, followed by water until there was a persistent faint cloudiness. The mixture was then seeded and the stirring rate increased; as more water (total 1 l.) was added during 1 hr., colourless crystals separated. An hour later the crystals were removed and washed with water. After drying, *benzyl α-hydroxyimino-β-oxobutyrate* had m. p. 76—78°; the yield was theoretical. A small sample recrystallized from benzene–*cyclo*hexane gave needles, m. p. 79—79·5° (Found: C, 60·0; H, 4·9. $C_{11}H_{11}O_4N$ requires C, 59·7; H, 5·0%).

Benzyl α-Amino-β-oxobutyrate Hydrochloride.—Stannous chloride dihydrate (100 g.) was dissolved in a mixture of ethanol (30 ml.) and hydrochloric acid (100 ml.; *d* 1·18) contained in a 2 l. flask, placed in a water-bath (16°) and fitted with a mechanical stirrer. To the solution was added finely powdered benzyl α-hydroxyimino-β-oxobutyrate (44·24 g., 0·2 mole) at such a rate that the temperature was just below 30°. When all the oxime had been added and the temperature had started to fall, the bath was warmed to 30°, stirring being continued for 1 hr. after all the solid had dissolved (extraction with light petroleum at this stage showed that less than 1% of the oxime remained). The solution was then cooled to 10° and ether (1 l.) was added. After addition of most of the ether the phases separated and the ethereal layer, which contained most of the stannous and stannic chloride, was discarded. After addition of water (100 ml.) the aqueous layer was again extracted with ether (3 × 500 ml.); at this stage the aqueous solution contained no tin, as judged by treatment with hydrogen sulphide. The yield of crystalline material depended on the speed at which water and excess of acid could be removed; titration showed that initially the yield of material having pK' 5·4 (see below) was theoretical. After ether-extraction, therefore, the liquid was transferred to an evaporating basin and left overnight in a desiccator (1 mm. Hg) containing sodium hydroxide. The crystals which resulted were removed by flotation with dry ether, followed by filtration and washing with dry ether in a filter-funnel protected from atmospheric moisture. (Only by this method could the product be obtained free from excess of hydrogen chloride and solid impurities. The crystals pass

readily into the ethereal phase on swirling of the aqueous suspension with ether; the resulting ethereal suspension can then be decanted before the crystals settle at the interface.) The desiccation and flotation were then repeated with the aqueous mother-liquor. After five such fractionations the yield of *benzyl α-amino-β-oxobutyrate hydrochloride* was 39·4 g. (81%) of colourless needles, m. p. 135—137° (decomp.), p*K′* 5·4 (Found: C, 53·9; H, 5·8; N, 6·0; Cl, 14·5. $C_{11}H_{13}O_3N,HCl$ requires C, 54·2; H, 5·8; N, 5·8; Cl, 14·6%).

Crystalline material obtained by rapid and complete removal of water, rather than by flotation into ether, was found by titration and titrimetric determination of chloride to contain 71% of the desired ester hydrochloride, exactly one equivalent of excess of hydrogen chloride, and 11·6% of an unidentified solid, insoluble above pH 2 and in organic solvents, which charred above 400° without melting. The pure dry hydrochloride is stable for several weeks, but the impure dry solid darkens in a few days. Solutions of the hydrochloride in hydrochloric acid slowly decompose, forming benzyl chloride (identified by its odour, and by extraction with ether to give an oil of b. p. 175—180°) and aminoacetone hydrochloride (identified chromatographically).

Benzyl 3 : 6-*Dimethylpyrazine*-2 : 5-*dicarboxylate*.—To a solution of the foregoing hydrochloride (2·44 g., 0·01 mole) in water (25 ml.) was added one equivalent of N-sodium hydroxide. The solution was left exposed to the air for a week, with occasional shaking. The white crystalline precipitate was removed, dried, and recrystallized from ether–light petroleum (b. p. 60—80°), yielding 1·66 g. (88%) of the desired *ester*, as colourless needles, m. p. 108°, $\lambda_{max.}$ 288 mμ (log ε 4·06) in methanol (Found: C, 69·9; H, 5·3; N, 7·5. $C_{22}H_{20}O_4N_2$ requires C, 70·2; H, 5·4; N, 7·4%).

Ethyl α-Chloroacetamido-β-oxobutyrate.—Crystalline ethyl α-hydroxyimino-β-oxobutyrate [9] (15·92 g., 0·10 mole) and chloroacetic anhydride (34·2 g.; 0·20 mole) were dissolved in acetic acid (50 ml.). This mixture was shaken under hydrogen for 5 hr. with palladized charcoal [12] (4 g.), by which time the theoretical quantity of hydrogen had been absorbed. After removal of the catalyst the acetic and chloroacetic acid and excess of anhydride were removed at 5 mm. from an oil-bath whose final temperature (120°) was maintained for 1 hr. The dark brown residue was dissolved in a hot 10% (v/v) solution (100 ml.) of ethanol in water and treated with charcoal. After filtration and cooling the water was extracted with chloroform (6 × 25 ml.). The chloroform extracts were dried and concentrated, and boiling light petroleum (b. p. 80—100°) was added. The solution, on slow cooling, yielded yellow crystals, m. p. 76—78°. These were recrystallized twice from ether, giving colourless needles (14·6 g., 66%) of the *chloroacetamido-ester*, m. p. 80—81° (Found: C, 43·3; H, 5·5; N, 6·7; Cl, 16·2. $C_8H_{12}O_4NCl$ requires C, 43·4; H, 5·5; N, 6·3; Cl, 16·0%).

Benzyl α-Chloroacetamido-β-oxobutyrate.—Benzyl α-amino-β-oxobutyrate hydrochloride (21·95 g., 0·09 mole) was added to a solution of chloroacetic anhydride (17·1 g., 0·10 mole) in acetic acid (100 ml.). To the mixture was added anhydrous sodium acetate (24·6 g., 0·3 mole), whereupon the temperature rose to 60°. The next day ether (250 ml.) was added and the precipitated sodium salts were removed by filtration. The ethereal solution was transferred to a separatory funnel and shaken with dilute sodium hydroxide solution; sufficient of the latter was added to bring the pH of the aqueous phase to between 5 and 6 one hour after the last addition. The aqueous phase was then separated and extracted twice with ether; the combined ethereal phases were washed with sodium hydrogen carbonate solution and finally with water. The ether was removed and the residue crystallized from methanol–water as light yellow clusters of needles, m. p. 97—98° (15·3 g., 60%). Recrystallized after solution in hot (90°) water, *benzyl α-chloroacetamido-β-oxobutyrate* formed colourless needles, m. p. 98° (Found: C, 55·3; H, 5·1; N, 4·9; Cl, 12·0. $C_{13}H_{14}O_4NCl$ requires C, 55·0; H, 5·0; N, 4·9; Cl, 12·5%).

Ethyl α-Acetamido-β-oxobutyrate.—This compound was prepared by catalytic reductive acetylation of the crystalline oxime as described.[9,22] The product, purified by recrystallization from dry ether–light petroleum (b. p. 60—80°) at −10°, had m. p. 48° (Albertson *et al.*[9] give m. p. 46—49°; Wiley and Borum [22] give m. p. 46—47·5°). By titration in water with sodium hydroxide, the apparent p*K′* corresponding with the ionization of the enol was found to be 8·72 (Found: equiv., 187·2. Calc. for $C_9H_{13}O_4N$: equiv., 187·2); by spectrophotometric titration a value of 8·1 was found [11] for the corresponding chloroacetyl compound.

Benzyl α-Benzyloxycarbonylamino-β-oxobutyrate.—Benzyl α-hydroxyimino-β-oxobutyrate (0·10 mole) was reduced with stannous chloride, and the reaction mixture was extracted with

[22] Wiley and Borum, *J. Amer. Chem. Soc.*, 1948, **70**, 1666.

ether, as described above. The residual aqueous solution was kept at 0° while small quantities of benzyl chloroformate (total 15 ml.) and 10N-sodium hydroxide (total 10 ml.) were added alternately in 2 hr. with vigorous stirring. The mixture was left overnight at room temperature and during the next day further small quantities of sodium hydroxide solution were added until the pH remained above 6. A precipitate (of the unidentified solid already mentioned) was allowed to remain, and the mixture was set aside for two weeks, crystallization of the desired product then commencing. After removal of crystals for seeding, the mixture was extracted with ether (5 × 100 ml.); the combined ethereal extracts were washed with dilute sodium carbonate and water, dried, and concentrated to about 50 ml. On addition of light petroleum (b. p. 100—120°) and seeding, yellow needles (m. p. 75—76°) were formed very slowly. After recrystallization from the same solvents and then twice from ethanol–water, *benzyl α-benzyloxycarbonylamino-β-oxobutyrate* formed colourless needles (18·8 g., 55% from the oxime), m. p. 77—77·5° (Found: C, 66·9; H, 5·7. $C_{19}H_{19}O_5N$ requires C, 66·8; H, 5·6%).

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287. α-Amino-β-keto-acids. Part II.[1] Rates of Decarboxylation of the Free Acids and the Behaviour of Derivatives on Titration.

By W. G. Laver, A. Neuberger, and J. J. Scott.

Rates of decarboxylation of α-amino-β-oxo-butyric and -adipic acid have been measured in ethanol and in water at various pH's. Both acids have maximum half-lives of about 20 min. in ethanol and about 8 min. in water at pH 0. The half-lives decrease with increase in pH, and at pH 7·0 are much less than 1 min., being too short to be measured by either the volumetric or the spectrometric techniques employed.

The pK' values of the amino- and acetamido-keto-esters, and their ultraviolet absorption spectra, show that both types of compound form an enol ion very readily. This behaviour is discussed in relation to factors influencing the decarboxylation of the free acids.

In the preceding paper,[1] experiments were described in which benzyl ester salts of two α-amino-β-keto-acids (amino-oxo-butyric and -adipic acid) were treated in several ways in order to remove the ester group. In all experiments rapid decarboxylation occurred and only the α-amino-ketones were isolated. From the volume changes during catalytic debenzylation it was apparent that absorption of hydrogen could be made to occur faster than decarboxylation. It is shown in the present paper that both absorption of hydrogen and evolution of carbon dioxide follow first-order kinetics, and that a transient accumulation of the free acid can be demonstrated spectrophotometrically. The results show that in aqueous solution at room temperature the two amino-keto-acids have similar half-lives, of the order of a few minutes in acid solution. Since the temperature and, in certain cases, the pH during reaction were not kept constant, the values obtained are considered to be only approximate. The emphasis of investigation was on the possibility of isolating the free amino-keto-acids for use in biological systems, rather than on obtaining precise velocity constants.

Experimental

Materials.—Preparation of the compounds is described in the preceding paper.[1]

Volumetric Procedure.—Hydrogenations in which volume changes were measured were conducted at room temperature (22—24°) and atmospheric pressure on quantities of 5—10

[1] Part I, Laver, Neuberger, and Scott, preceding paper.

mmoles. The reaction flask had a side-arm with a stop-cock. In addition to being used for introduction of the material to be hydrogenated, the side-arm was connected by a flexible tube to a series of wash-bottles containing aqueous barium hydroxide when it was desired to determine the carbon dioxide evolved; a stream of hydrogen could then be passed through the apparatus while the flask was being shaken.

The required weight of 10% palladized charcoal [2] was suspended in the solvent and equilibrated with hydrogen before addition of the compound to be reduced. However, since methanol or ethanol may inflame if added to the catalyst in the presence of air, these solvents were added to the catalyst after the apparatus had been filled with hydrogen. In all cases equilibration was deemed sufficient when the hydrogen uptake was less than 0·2 ml./min.; this rate or less was attained after 20 minutes' shaking.

Spectrophotometric Procedure.—The following procedure was used to follow the change of spectrum in ethanol or in water containing 10% v/v of ethanol. Palladized charcoal (0·15 g.) were equilibrated first with nitrogen and then with hydrogen. A solution in ethanol (10 ml.) of about 0·3 mmole of α-benzyl hydrogen α-amino-β-oxo-adipate hydrochloride monomethanol solvate, or of the toluene-*p*-sulphonate, was then added rapidly and the mixture was shaken under hydrogen for 1 min. The catalyst was then rapidly filtered off under pressure through a sintered-glass disc; 2 ml. of the filtrate were mixed with 18 ml. of water or ethanol, and sufficient was at once transferred to an absorption cell; the pH of the remainder was measured by means of a glass electrode. Measurements of the absorption at 257·5 mμ were made in a Carey recording spectrophotometer (10 cm. cell) or in a Unicam SP. 500 spectrophotometer (1 cm. cell). The initial optical densities were only about 70—80% of the calculated values extrapolated to zero time. By using solutions of the unchanged benzyl ester, this was found to be due to retention of up to a third of the absorbing material on the catalyst. The effect was significant only when the weight of catalyst used was as great as that of ester.

The light-absorption constants were obtained from measurements with the Unicam SP. 500 spectrophotometer.

Determination of Velocity Constants.—The rates of hydrogenolysis followed first-order kinetics, and were proportional to the amount of catalyst present (see Fig. 1 and Table 1). The subsequent decarboxylation of the free acid is a first-order process, so the overall kinetics are those of two first-order reactions whose rate equations are readily integrable.

If the quantities of benzyl ester, free acid, and decarboxylated product are b, c, and d respectively after t min., then:

$$b = B \exp(-k_1 t) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where B is the initial quantity of ester;

$$c = B \frac{k_1}{k_2 - k_1} [\exp(-k_1 t) - \exp(-k_2 t)] \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

and

$$d = B - (b + c) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

k_1 and k_2 being the respective rate constants for debenzylation and decarboxylation.

(a) *Volumetric determinations of* k_2. Most of the measurements of b, c, and d were made, not directly, but by following the changes in volume of the gas phase as hydrogen was absorbed and carbon dioxide evolved. If V is the volume of hydrogen equivalent to B, then:

$$(V - v_H + v_O)/V = (b + d)/B \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where v_H and v_O are the volumes absorbed or evolved after t min., and

$$(V - v_O)/V = (b + c)/B \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

The sum, $(b + d)$, can therefore be evaluated from the observed changes in volume, while $(b + c)$ can only be evaluated volumetrically by determination of v_H. It follows from equations (1) and (3) that log $(b + d)$ will initially be effectively linear in t with slope k_1 provided $k_2 < k_1$. If k_2 is finite then it is always theoretically possible to make $k_2 < k_1$ by increasing the amount of catalyst; so k_1 can generally be evaluated and hence v_H and, by difference, v_O. It also follows from equations (1) and (2) that, for $k_2 < k_1$, log $(b + c)$ will eventually become linear in t, with

[2] Harington and Randall, *Biochem. J.*, 1931, **25**, 1917.

slope k_2, after an initial period with slope $< k_2$, during which b is being converted into c, but with little change in $(b + c)$.

The linear phase of log $(b + d)$ was conveniently extended as a result of the solubility of carbon dioxide in the non-gaseous phases, so that v_0 could not be obtained at low values of t. Because of this partition of carbon dioxide between the phases, the volume of the gas phase did not return completely to its original value when reaction was virtually complete. It was assumed that the non-gaseous phases were saturated with an approximately constant volume of carbon dioxide once the sum $(b + d)$ had started to increase (see Fig. 1). Accordingly, for evaluation of v_0 at sufficiently large values of t, the difference between the initial and the final volume was added to the difference between $(V - v_H + v_0)$ and $(V - v_H)$. The validity of this approximation with respect to the determination of k_2 was borne out by direct determination as described below. However, the absolute values of $(b + c)$ obtained volumetrically were clearly too low (see Fig. 1), and it was never possible to recover more than about 70% of the carbon dioxide presumably liberated. Also, if $k_1 < k_2$, then k_2 cannot be calculated from the slope of log $(b + c)$, which will then approximate to k_1.

(b) *Spectroscopic determination of* k_2. Dimethyl α-amino-β-oxoadipate hydrochloride absorbed about five times more strongly in the region 250—265 mμ than the decarboxylated product, δ-aminolævulic acid, which possesses only the absorption [3] expected from the carbonyl chromophore. Decarboxylation, following removal of the α-ester group, is therefore attended by a decrease in optical density of the solution provided no other reactions take place. For the benzyl ester hydrochloride, however, this decrease in absorption is only about 20%, and for the toluene-*p*-sulphonate about 14%, because absorption due to the benzyl chromophores is virtually unaltered by hydrogenolysis. Extinction coefficients of the relevant compounds are included in Table 2. Even for the benzyl ester toluene-*p*-sulphonate, the changes in absorption sufficed to permit direct evaluation of k_2: by analogy with equation (5),

$$(b + c)/B = (D_t - D_\infty)/(D_0 - D_\infty) \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

where D_0, D_t, and D_∞ represent respectively the optical densities at 257·5 mμ initially, after t min., and finally. Further, by employing a large excess of catalyst, b could be made negligible; under such conditions determination of δ-aminolævulic acid at the end of the experiment showed that all the ester groups must have been cleaved before the spectrophotometric measurements were started.

δ-Aminolævulic Acid.—(a) *Isolation after hydrogenation.* α-Benzyl hydrogen α-amino-β-oxoadipate toluene-*p*-sulphonate (3·277 g.) in absolute ethanol (100 ml.) was hydrogenated in the presence of palladized charcoal (0·25 g.). The volume changes are shown in Fig. 1. When reaction had ceased the catalyst was removed and ether was added. The crystals formed had m. p. 182—182·5°, mixed m. p. 181·5—182° with δ-aminolævulic acid toluene-*p*-sulphonate (m. p. 182·5—183°). The latter was prepared from the hydrochloride by metathesis on an ion-exchange column (Deacidite FF in the toluene-*p*-sulphonate form), as described for benzyl hydrogen amino-oxoadipate in the preceding paper.[1] On examination by paper chromatography in butan-1-ol–water–acetic acid (63 : 27 : 10; upper phase), the product isolated after hydrogenation showed a single spot (R_F 0·5) identical with that of δ-aminolævulic acid toluene-*p*-sulphonate.

(b) *Determination after hydrogenation.* α-Benzyl hydrogen α-amino-β-oxoadipate hydrochloride methanol solvate (100 mg.) in absolute ethanol (10 ml.) was hydrogenated with palladized charcoal (150 mg.) for 1·5 min. The mixture was then rapidly filtered and 0·2 ml. of filtrate, corresponding to 6·0 μmoles of benzyl ester, was diluted with 50 ml. of 0·1M-potassium phosphate of pH 7·4, and the absorption was read immediately in a 1 cm. cell at 260 and 273 mμ. The optical densities of the solution were 0·030 and 0·025 and did not alter with time; the optical density of the starting material at the same concentration and pH was initially 0·420 at 273 mμ. The amount of aminolævulic acid present in the buffered solution after hydrogenation was estimated by the picrate method of Shuster [4] as modified by Laver, Neuberger, and Udenfriend [5] and also by the method of Mauzerall and Granick,[6] giving 5·4 and 5·75 μmoles respectively.

[3] Scott, Ph.D. Thesis, London, 1954.
[4] Shuster, *Biochem. J.*, 1956, **64**, 101.
[5] Laver, Neuberger, and Udenfriend, *ibid.*, 1958, **70**, 4.
[6] Mauzerall and Granick, *J. Biol. Chem.*, 1956, **219**, 435.

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Catalytic Hydrogenation of α-Benzyl Hydrogen α-Acetamido-β-oxoadipate.—The ester (1·54 g.) in absolute ethanol (50 ml.) was added to palladized charcoal (1 g.) in ethanol (25 ml.) under hydrogen. Uptake of hydrogen was 1 equiv. in 5 min. Slow evolution of carbon dioxide was detectable after 16 min. in a parallel experiment. After 15 min. the catalyst was removed and the filtrate evaporated to dryness under reduced pressure in an air-bath. The residue had m. p. 67—80° without evolution of gas, raised to 93—95·5° after recrystallization from ethanol–ether, mixed m. p. 91·5—98° with δ-acetamidolævulic acid [7] (m. p. 92—94°). One equivalent of sodium hydroxide was required to make an aqueous solution of the product alkaline to phenolphthalein.

In a second experiment one equivalent of anhydrous sodium acetate in ethanol was added after 5 min. in such a way as to cause no change in the total volume of the system. Evolution of carbon dioxide was then rapid, with $t_{\frac{1}{2}} \sim 15$ min.

Spectrophotometric Titration.—The acetamido-compounds listed in Table 2 were titrated by using sodium phosphate buffer solutions (0·1M with respect to P). For the amino-keto-ester salts a special procedure was necessary as the optical density of solutions of these compounds sufficiently dilute for spectroscopic study decreased linearly with time, but independently of pH and, therefore, of the initial density; the density at 273 mμ became negligible after 1 hr. The required pH was obtained either by mixing a solution of the ester salt with a 0·1M-buffer solution or else by dilution of a 0·10M-solution of the ester salt to which sufficient 0·10M-sodium hydroxide had been added; in the latter case the ionic strength was very low and the results were not used in calculating the pK' values reported; the pH was always checked potentiometrically after absorption measurements. It was found that the rate of fading was related to the nature and concentration of the buffer in the following way: diethylbarbiturate (veronal) > phosphate > acetate > no buffer; concentrated > dilute. The fading was only important at great dilution ($<10^{-5}$M) since the same absorption and rate of fading were found after dilution of a freshly made 0·05M-solution as with one which had remained at the selected pH for 1 hr. before dilution (cf. Fig. 4). For measurement of pK' values density readings were made every minute for 20 min. after dilution of a strong solution of ester salt with a buffer solution; extrapolation of the straight line, obtained by plotting on Cartesian co-ordinates, evaluated D_{273} at zero time. Similar values at zero time were obtained by using different buffer systems at the same pH.

The significance of the time-dependent spectroscopic changes is not clear. The changes were not reversed by acidification to pH 1 and re-neutralizing, and no absorption due to a pyrazine ($\lambda_{max.}$ 290; ε 10,000 [1]) was observed until after the diluted solution had been exposed to the air for several days.

Results and Discussion

Two typical sets of observations made by the volumetric procedure are shown in Fig. 1, together with the graphical method of measuring the half-lives corresponding to k_1 and k_2. Comparison of curves *B* and *D* shows that the amount of catalyst used did not affect the rate of decarboxylation. Some determinations by the spectrophotometric procedure are shown in Fig. 2; under these conditions k_1 is made very large, and changes in absorption are due only to decarboxylation. The results of a series of such measurements in ethanol and in water at several pH values are given in Table 1. It is evident that there is very little difference in stability between the two α-amino-β-oxo-acids studied, either in ethanol or in water.

In the preceding paper it was reported that, while hydrogenation of ethyl α-phenylhydrazono-β-oxobutyrate or its *N*-acetyl derivative, in organic solvents containing two or more equivalents of hydrogen chloride, gave the amino-keto-ester in good yield, similar treatment of the benzyl esters gave aminoacetone. It may be seen from Fig. 3, curve *A*, that in such cases no transient accumulation of the amino-keto-acid was demonstrable. As the free phenylhydrazono-acid is a relatively stable compound it seems probable that the aniline formed in the reaction catalyses [8] the decarboxylation of the amino-acid to such an extent that its rate of decomposition is greater than both the rates of uptake of

[7] Neuberger, Scott, and Shuster, *Biochem. J.*, 1956, **64**, 137.
[8] Widmark and Jeppsson, *Skand. Arch. Physiol.*, 1922, **42**, 43.

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hydrogen even when the concentration of aniline, as opposed to anilinium ion, is low; this conclusion is supported by the values in Fig. 3, curve *C*, from which it is evident that from the corresponding oxime the amino-keto-acid can accumulate. Three mols. of hydrogen were absorbed. The faster rate (Fig. 3, curve *B*) represents debenzylation to form eventually the free phenylhydrazono-acid,[1] as was shown by examination of the ether-soluble material present when hydrogenation was stopped after uptake of about one mol.; 78% of the theoretical amount of the free acid having the correct m. p. was so isolated. The slower rate represents cleavage of the phenylhydrazono-group with uptake of two

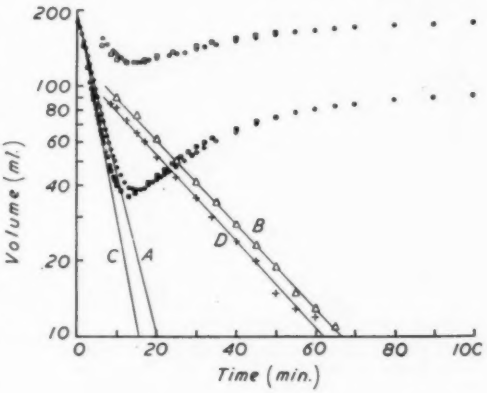

FIG. 1. *Determination of the rate of decarboxylation of amino-oxoadipic acid by the volumetric method.*

The results are derived from two experiments in ethanol, each with α-benzyl hydrogen α-amino-β-oxoadipate toluene-*p*-sulphonate equiv. to 180 ml. of hydrogen, with (1) 160 and (2) 250 mg. of palladized charcoal. In the notation of equation (4): $V = 180$; $b + d$ observed in expt. (1) ●, and in expt. (2) ■; $b + d$ corrected for retention of CO_2 in non-gaseous phases, in expt. (1) ○, and in expt. (2) □; hence $b + c$, in expt. (1) △, in expt. (2) +. k_1 and k_2 are evaluated, in terms of $t_{\frac{1}{2}}$, from the slopes of curves *A* and *B* [expt. (1)] and curves *C* and *D* [expt. (2)] (see Table 1).

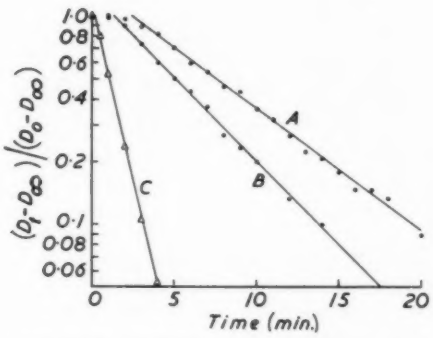

FIG. 2. *Determination of the rate of decarboxylation of amino-oxoadipic acid by the spectroscopic method.*

Aqueous solutions of the free acid were prepared as described. *A*, pH 3·30; *B*, pH 3·50; *C*, pH 5·0. See equation (6) and Table 1.

equivalents of hydrogen and output of one equivalent of carbon dioxide. 0·72 mol. of carbon dioxide was recovered as barium carbonate after the volume changes had ceased. Reductive cleavage of both the phenylhydrazono- and the hydroxyimino-group was found, from tests with the corresponding ethyl ester, to proceed at a single first-order rate. This suggests that adsorption of a molecule of the $>C=N-$ compound on the catalyst is in effect followed by uptake of two equivalents of hydrogen before significant desorption takes place.

It appears from measurements of rates of decarboxylation at different pH values (Table 1) that the half-life of either amino-keto-acid decreases with increase in pH up to pH 5. At pH 7·0 and 7·4 the half-life was too short to be measured by either the volumetric or the spectrophotometric method. These values suggest that, while all forms of the acid (I; R = H) are unstable, one or more of the species formed on ionization is even less stable. Qualitatively, a similar decrease in stability on dissociation was observed for the corresponding *N*-acetyl free acids, the half-life in ethanol decreasing from several hours to about 15 min. when sodium acetate was added to the solution.

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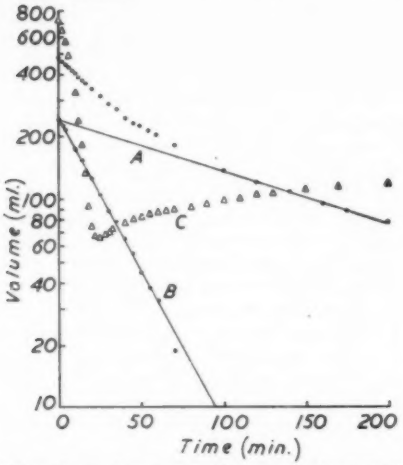
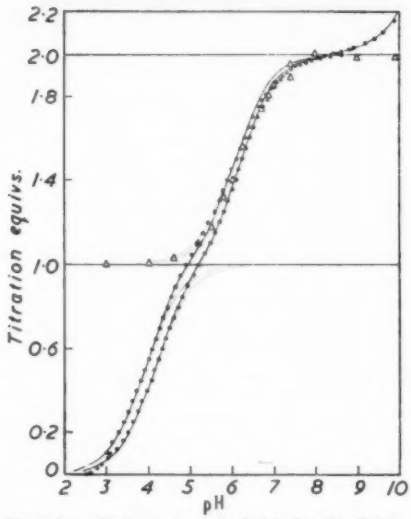
FIG. 3. *Hydrogenolysis of benzyl α-(N-acetyl phenylhydrazono)- and α-hydroxyimino-β-oxobutyrate.*



The volume change on hydrogenation is plotted analogously to that in Fig. 1. The ester indicated (10 mmoles) was hydrogenated in benzene containing dry HCl (30 mmoles) and palladized charcoal (1 g.). *N*-Acetylphenylhydrazone, observed values ○; curve *A* gives the slower rate of hydrogen uptake ($t_{\frac{1}{2}}$ 120 min.) and the difference is curve *B* (●), giving the faster rate ($t_{\frac{1}{2}}$ 21 min.). Oxime observed values △. Under the conditions of the experiments 10 mmoles of hydrogen measured 240 ml.

FIG. 4. *Potentiometric and spectrophotometric titration of α-benzyl hydrogen α-amino-β-oxoadipate toluene-p-sulphonate.*



Titration of the ester salt (0·05M) with 0·05N-NaOH, ●; the right-hand continuous and dotted lines give the theoretical values for pK' 4·15, 6·20 and, in part, 10·58. ○ represents the reverse titration with 0·05N-HCl after addition of 2·0 equivalents of 0·10N-NaOH; the left-hand continuous and dotted lines give the theoretical values for pK' 3·90 and 6·10. △, spectrophotometric titration (cf. Table 2); (D_{273} at pH 9) − (D_{273} at pH 3) = 0·8 (= 1 equiv.).

TABLE 1. *Approximate maximum half-lives (min.) of α-amino-β-oxo-acids.*

Solvent	pH	$t_{\frac{1}{2}}$ of free acid	$t_{\frac{1}{2}}$ of debenzn.	Solvent	pH	$t_{\frac{1}{2}}$ of free acid	$t_{\frac{1}{2}}$ of debenzn.
α-Benzyl hydrogen α-amino-β-oxoadipate							
Toluene-p-sulphonate				*Hydrochloride methanol solvate*			
EtOH	—	18·0[a]	4·6[a]	EtOH	—	15·0[b]	⩽1
	—	17·5[a]	3·1[d]	H_2O	~0[e]	>5<8[b,f]	⩽1
	—	18·0[b]	⩽1		3·30	5·0[b]	⩽1
H_2O	2·5	6·7[a]	5·0		3·50	3·7[b]	⩽1
	3·28	5·2[b]	⩽1		5·0[g]	0·85[g]	⩽1
					7·4	~0[b,h]	⩽1
Benzyl α-amino-β-oxobutyrate hydrochloride							
EtOH	—	22[a]	2·5	H_2O	7N-HCl	8·1[a]	1·85
					0·1N-HCl	7·7[a]	1·5
					4·1	3·5[a]	2·0
					4·9	1·85[a]	1·35

[a] Volumetric method (Fig. 1). [b] Spectroscopic method (Fig. 2). [c, d] Using respectively 180 and 250 mg. of palladized charcoal. [e] N-HCl. The curve from which these values were obtained was not quite linear. [g] 0·05M-Buffer (acetic acid–sodium acetate). [h] Measurements were made at both 260 and 273 mμ.

Dissociation constants of the amino-keto-esters and their derivatives in water were determined either potentiometrically or by spectrophotometric titration. The results, expressed as pK' values of the relevant acidic groups, are summarized in Table 2, together with certain light-absorption constants.

For the acylamino-compounds listed in Table 2, pK' values of about 8 represent ionization of the enol, since no other group would be expected to be dissociating at this pH and also because the ionization is accompanied by a great increase in absorption at 276 mμ.

TABLE 2. pK' *values and absorption data for derivatives of* α-*amino*-β-*oxo-acids.*

Compound	pK' (22°) 1	2	3	Solvent	pH	$\lambda_{max.}$ (mμ)	ε
Et_2 α-amino-β-oxoadipate HCl				EtOH		257·5 [a]	98
	5·82 [c]	10·4 [c]		H_2O	3·9	260 [a]	99 [b]
	5·82 [d]				7·4	273	7600
α-CH_2Ph H α-amino-β-oxo-adipate HCl,MeOH	4·15	6·20 [c]	10·6 [c]	EtOH		257·5	394
		6·15 [d]		H_2O	3·3	257·5	394
					8·0	273	7910 [e]
α-CH_2Ph H α-amino-β-oxo-adipate toluene-*p*-sulphonate	4·15	6·20 [c]	10·6 [c]	EtOH		257·5	581
α-CH_2Ph H α-acetamido-β-oxo-adipate				EtOH		257	1280
				EtOH–NaOH [f]		276	23,100
	4·35	8·90 [c]		H_2O	6·3	260	256 [g]
		8·90 [d]			11·0	276	23,000
α-CH_2Ph H α-chloroacetamido-β-oxoadipate				EtOH		257	1212
				EtOH–NaOH [f]		276	21,700
CH_2Ph (or Et) α-amino-β-oxo-butyrate HCl	5·20 [c]	11·0 [c]			Not measured accurately		
Et α-chloroacetamido-β-oxo-butyrate				EtOH–NaOH [f]		274	17,200
	8·30 [c]			H_2O	6·0	252	550
	8·10 [d]				11·5	273	12,700
δ-Aminolævulic acid HCl [3]	4·05	8·90 [c]		H_2O	2·0	(257·5)	21 [h]

[a] Shoulder. [b] ε_{273} 89. [c] Potentiometric determination. [d] Spectroscopic determination. [e] Fig. 4. [f] 10^{-5}M-NaOH; absorbing compound $7·5 \times 10^{-6}$M. [g] ε_{276} 146. [h] This value is not $\lambda_{max.}$ but is given for comparison with $\varepsilon_{max.}$ of the α-amino-β-oxo-acids.

Similar changes of spectrum with pH were observed [9] in a series of the closely related penaldate esters ($\lambda_{max.}$ 265—270; ε *ca.* 15,000; apparent pK'_{enol} 6·3—6·6).[10] The true pK'_{enol} values must however be substantially lower than those observed, as the enol–keto-equilibrium in water favours the ketonic forms.

Direct titration of the toluene-*p*-sulphonate of the ester (I; R = CH_2Ph; R′ = CH_2·CO_2H) showed the presence of three ionizing groups. pK_1' has the value expected for the δ-CO_2H group, being similar to that of δ-aminolævulic acid; pK_3' presumably represents formation of structures equivalent to the free amino-enol ion, ·C(O⁻):C(NH_2)·. Spectrophotometric titration showed the presence of only one operative group between pH 1 and 11, having the same value as pK_2'; measurements were made as described above, at 273 mμ, the value of $\lambda_{max.}$ for the absorbing species predominating at higher pH. Similarly the diethyl ester had two ionizing groups, only pK_1' being spectroscopically operative. In both cases potentiometric titration was almost completely reversible over a range of pH which included the spectroscopically operative pK' (Fig. 4) provided back-titration was carried out at once; solutions exposed to the air for several days at pH > (pK + 1) became cloudy and a crystalline precipitate of a sodium salt of the corresponding pyrazine [1] was formed slowly as the water evaporated.

Comparison with $\lambda_{max.}$ of the acylamino-compounds (Table 2) suggests the formation of an enol ion on titration of esters (I; R = alkyl), but $\varepsilon_{max.}$ is only one-half to one-third of the expected value. Without considerable further study it is not possible to define

[9] Merck and Co., Inc., 1944, Report 30; cited in "The Chemistry of Penicillin," p. 501, ed. Clarke, Johnson, and Robinson, Princeton Univ. Press, 1949.
[10] Eli Lilly and Co., 1944, Report 17; cited in *op. cit.*, p. 501.

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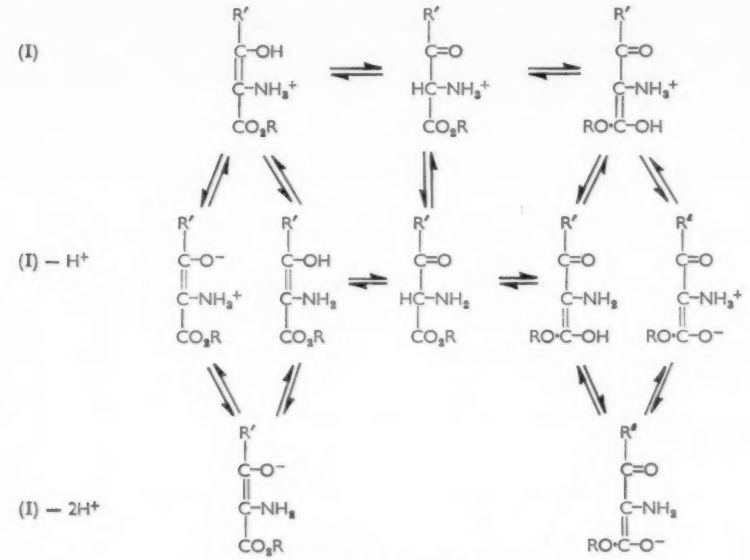

Only *cis*-forms are shown.

pK_1' of the diester (I; R = Et, R′ = $CH_2{\cdot}CO_2Et$) or pK_2' of the monoester (I; R = CH_2Ph, R′ = $CH_2{\cdot}CO_2H$) with certainty in terms of the many equilibrium constants possibly involved. The equilibria must be complex because of the possibilities introduced, not only by keto–enol tautomerism, but also by the different acidities to be associated with the *cis*- and *trans*-forms of the amino-enol. Possible contributants to the equilibria are shown in the accompanying formulæ; only those forms are shown in which charges are localized on oxygen or nitrogen atoms. As the pK' in the region pH 10—11 is spectroscopically inoperative, it may be concluded that there is little change above pH 9 in the proportion of species having the αβ-unsaturated carbonyl structure. A net loss of a proton between pH 4 and 8 results therefore in complete enolization. The ratio of uncharged to zwitterionic enolic forms depends on a number of factors which cannot at present be assessed; in addition to those already mentioned, formation of five-membered rings involving hydrogen-bonds, such as those proposed for tropolone,[11] may have to be considered; in the present case the hydrogen-bond would lie between the amino-group and one of the two carbonyl groups. In view of the complexity of the system it is not advisable to draw conclusions from the marked decrease in value of ε_{273} from that for the corresponding *N*-acetyl compounds, although it may be noted that differences of a similar order have been observed in the case of the *K*-bands of *cis*- and *trans*-cinnamic acid.[12]

Table 1 shows that the half-life of amino-oxobutyric acid diminishes only slightly on rise of pH from <0 to about 1. The pK' of the carboxyl group would be expected to lie in the range 1—1·5 from consideration of the relevant pK' values of glycine and acetoacetic acid. Carbon dioxide must therefore be lost both from the mono-cation and from the zwitterion, $R{\cdot}CO{\cdot}CH(NH_3^+){\cdot}CO_2^-$, and at about the same rate. It may also be seen that the half-lives of both acids decrease sharply above pH 3 indicating that, above this pH, a species formed from the zwitterion by loss of a further one or two protons is very unstable. This species cannot be identified from the results so far obtained. Both the mono-cation and the zwitterion mentioned above possess a charged α-amino-group, and

[11] Cook and Loudon, *Quart. Rev.*, 1951, **5**, 99.
[12] Gillam and Stern, "Electronic Absorption Spectroscopy in Organic Chemistry," 1st edn., Arnold, London, 1954, p. 233.

the mechanism of decarboxylation may be similar to that proposed for the trichloroacetate ion,[13] rather than by the generally accepted mechanisms of decarboxylation of undissociated β-keto-acids.[14] As the very much less stable species cannot be identified, no mechanism is proposed to account for loss of carbon dioxide at less acid pH values.

The fact that decarboxylation is virtually instantaneous at neutral pH is of biochemical interest and indicates that amino-oxoadipic acid cannot be isolated from a biological system.

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[*Received, October 28th*, 1958.]

[13] Verhoek, *J. Amer. Chem. Soc.*, 1934, **56**, 571; 1945, **67**, 1062; Hall and Verhoek, *ibid.*, 1947, **69**, 613; Cochran and Verhoek, *ibid.*, p. 2987; Auerbach, Verhoek, and Henne, *ibid.*, 1950, **72**, 299; Johnson and Moelwyn-Hughes, *Proc. Roy. Soc.*, 1940, *A*, **175**, 118.

[14] Pedersen, *J. Phys. Chem.*, 1934, **38**, 559; Westheimer and Jones, *J. Amer. Chem. Soc.*, 1938, **60**, 595; see also Brown, *Quart. Rev.*, 1951, **5**, 131.

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288. *The Configuration of Heterocyclic Antimony Compounds. Part IV.* Attempts to obtain 9-Stibiafluorene Oxides for Resolution Experiments.*

By I. G. M. CAMPBELL and A. W. WHITE.

The considerable optical stability of 9-stibiafluorenes led to the hope that oxides of such compounds could be similarly resolved, but they appeared to form dihydroxides which could not be dehydrated.

EARLIER Parts * describe the synthesis and optical resolution of substituted stibiafluorenes in which the antimony atom is tervalent, and we proposed to extend the work to the quadricovalent stibiafluorene oxides, since optical resolution of oxides of the type abcMO, where M is a member of Group VB, has been achieved only when M is nitrogen or phosphorus. Attempts to resolve arsine oxides have uniformly failed except for 2-carboxy-10-phenylphenoxarsine 10-oxide,[1] and the enantiomers of this oxide, $[\alpha]_D$ +36° and −29° (in dilute ammonia), are readily racemised, in striking contrast to the marked optical stability of the unoxidised phenoxarsine. In commenting on this, Lesslie suggested that the most probable cause was the hydration of the oxide to dihydroxide, a possibility which has been referred to more recently [2] where the failure to isolate enantiomers is ascribed to the possible conversion $(abcAs{\cdot}OH)X \longrightarrow abcAsO$ through the dihydroxide $abcAs(OH)_2$. The dihydroxides, if covalent, would be expected to possess the symmetrical trigonal bipyramidal configuration but, if ionic, would be tetrahedral and give a tetrahedral oxide.

The considerable optical stability of the 9-stibiafluorenes [3] encouraged us to investigate the oxides of this type of molecule, particularly as in the synthesis of the unsymmetrically substituted compounds, the product of cyclisation of the 2-diphenylylstibinic acid (I) was presumed to be the oxide (II), although this intermediate was usually reduced without characterisation to the corresponding stibiafluorene. Only in one case was the intermediate purified by crystallisation (from ethyl acetate), and then analysis indicated it to be the oxide (II; R = H, $R' = CO_2Et$)[4]. However, on examining the product of cyclisation of the acids (I; R = OMe, $R' = CO_2Et$; and I; $R = O{\cdot}CH_2CO_2Et$, R' = Me), it was found that the cyclic product was, in each case, the dihydroxide (III). These

* Part III, *J.*, 1955, 1662.

[1] Lesslie, *J.*, 1939, 1050.
[2] Hart and Mann, *J.*, 1955, 4107.
[3] (*a*) Campbell and Poller, *J.*, 1956, 1195; (*b*) Campbell and Morrill, *J.*, 1955, 1662.
[4] Campbell, *J.*, 1952, 4448.

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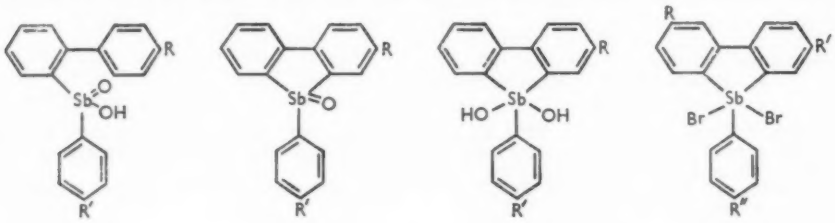
dihydroxides did not tend to lose water to form the oxides, despite prolonged heating at 100° under vacuum.

In an attempt to avoid the use of acetic anhydride which might encourage the retention of hydroxyl groups by acetylation, cyclisation was attempted with " polyphosphoric acid," a very successful reagent in the arsenic series;[3a] but when the stibinic acid (I;



R = O·CH_2·CO_2Et, R′ = Me) was so treated, extensive decomposition occurred and 4-diphenylyloxyacetic acid, m. p. 190°, was the sole product identified.

Another method recommended for the preparation of stibinic oxides is treatment of stibine dibromides with alcoholic alkali,[5] and this method was applied to 2-carboxy-9-*p*-tolyl-, 3-bromo-9-*p*-tolyl- and 3-bromo-9-*p*-ethoxycarbonylphenyl-9-stibiafluorene. The dibromides (IV) separated readily on addition of bromine to the stibiafluorenes in chloroform, carbon tetrachloride, or benzene, but possessed the property, which seems to be characteristic of stibine halides,[6] of retaining solvent of crystallisation. Consistent analyses were obtained only when carbon tetrachloride was used for both preparation and recrystallisation. Treatment of the dibromides (IV; R = Br, R′ = H, R″ = CO_2Et) and (IV; R = Br, R′ = H, R″ = Me) with warm alcoholic alkali gave oxides which retained two molecules of water even after prolonged vacuum-drying at 100°. [The dibromide (IV; R = H, R′ = CO_2H, R″ = Me) gave an insoluble product, m. p. >310° and apparently polymeric.]

As three of the five compounds investigated yield products of this composition it is tempting to suggest that these are solid complexes of the structure $H^+[Ar_3Sb(OH)_3]^-$, and the solubility of the compound from the dibromide (IV; R = Br, R′ = H, R″ = Me) in dilute aqueous alkali supports the idea. Triphenylstibine dihydroxide, $Ph_3Sb(OH)_2$, also dissolves in dilute alkali and may form the same type of salt, $Na^+[Ph_3Sb(OH)_3]^-$, the corresponding complex acid losing water on isolation.

A final attempt to obtain an oxide by treatment of 2-carboxy-9-*p*-tolyl-9-stibiafluorene in glacial acetic acid with hydrogen peroxide again produced insoluble material, m. p. >310°, and when the (—)-isomer was used, complete racemisation occurred.

The tendency for the stibiafluorene oxides to form extremely stable hydrates is evidently shared by triarylstibine oxides in general. For example, triphenylstibine oxide has apparently never been isolated; the dihydroxide is stable up to its m. p., 212°. Further, the formulæ given for many such " oxides " show that, to comply with analysis, one and occasionally more than one molecule of water has to be included.[8] In the stibiafluorene series this property is so pronounced that successful optical resolution of a member seems remote, for, even if a true oxide could be prepared, the process of resolution, involving salt formation and decomposition, would almost certainly convert the oxide into the hydrated form, and consequently no attempts have been made.

[5] Christiansen, " Organic Derivatives of Antimony," Chem. Catalog Co., 1925, p. 38.
[6] Worrall, *J. Amer. Chem. Soc.*, 1930, **52**, 2046; Campbell and White, *J.*, 1958, 1184.
[7] May, *J.*, 1910, **97**, 1956.
[8] Newton Friend, " Textbook of Inorganic Chemistry," Vol. XI, Part III (Goddard), Chas. Griffin, 1936, pp. 203–209.

Experimental

9-p-Ethoxycarbonylphenyl-2-methoxy-9-stibiafluorene 9-Dihydroxide.—*p*-Ethoxycarbonylphenyl-4′-methoxy-2-diphenylylstibinic acid (7·5 g.) was cyclised as previously described [3b] and the product (6·7 g.) was extracted with acetone. The insoluble residue (0·6 g.), m. p. 285—290° (decomp.), was the *dihydroxide* of the free acid (Found: C, 52·4; H, 4·0. $C_{20}H_{17}O_5Sb$ requires C, 52·3; H, 3·8%). The portion soluble in acetone was regained, crystallised from ethyl acetate–ethanol, and proved to be the *ester dihydroxide*, m. p. 185—188° (Found: C, 54·6; H, 4·3; Sb, 24·9. $C_{22}H_{21}O_5Sb$ requires C, 54·2; H, 4·3; Sb, 25·0%). This compound (0·5 g.) was hydrolysed by boiling with ethanolic potassium hydroxide (20 ml., 4%) for 0·5 hr. and the gelatinous precipitate obtained on acidifying the diluted solution was dried (0·35 g.) and found to be identical with the free acid obtained directly from the ring closure (Found: C, 51·9; H, 4·0%). Proof that the ester and acid were both ring compounds, and not the uncyclised stibinic acids which have the same molecular formulæ, was obtained by reduction to the corresponding stibiafluorenes, m. p. 147° and m. p. 231°, respectively. For comparison, the uncyclised stibinic acid was reduced under the same conditions and gave p-*ethoxycarbonylphenyl-4′-methoxy-2-diphenylylstibinous chloride*, m. p. 96° (Found: C, 54·4; H, 4·0. $C_{22}H_{20}O_3ClSb$ requires C, 54·0; H, 4·1%).

2-Carboxymethoxy-9-p-tolyl-9-stibiafluorene 9-Dihydroxide.—Ring closure of the required stibinic acid (5 g.), as in the previous experiment, gave a mixture (4·5 g.) which on crystallisation gave fractions of indefinite m. p. ranging from 200° to 260°. Reduction proved that this material was largely the cyclic compound, as 2-ethoxycarbonylmethoxy-9-*p*-tolyl-9-stibiafluorene was obtained in 70% yield, m. p. 132—133°, alone or mixed with an authentic sample.[3b] The crude product (3·3 g.) in ethanol (110 ml.) was boiled with 10% aqueous potassium hydroxide (33 ml.) for 0·5 hr., and the diluted solution acidified to Congo Red with dilute sulphuric acid. The dry product was purified by solution in aqueous sodium hydrogen carbonate and reprecipitation, as no suitable solvent could be found for crystallisation. After drying at 100°/15 mm. for prolonged periods, the acid had m. p. 276° (decomp.), and appeared to be the *dihydroxide monohydrate* (Found: C, 51·7; H, 4·7. $C_{21}H_{19}O_5Sb,H_2O$ requires C, 51·4; H, 4·3%). Repetition of the ring closure gave a solid which, after crystallisation from ethanol–chloroform, proved to be the *ester dihydroxide*, m. p. 148—150° (decomp.) (Found: C, 54·5; H, 4·5. $C_{23}H_{23}O_5Sb$ requires C, 55·1; H, 4·6%). Hydrolysis of this ester gave an acid which was crystallised once from ethanol and had m. p. 276° (decomp.), but could not be recrystallised from the same solvent (Found: C, 51·7; H, 4·2%).

Attempted Cyclisation by Means of "Polyphosphoric Acid."—The stibinic acid (I; R = O·CH_2·CO_2Et, R′ = Me) (1 g.) was added to polyphosphoric acid (5 g.), warmed to 160° for 3 min., cooled, and poured into water (100 ml.). The product (0·56 g.) was extracted with acetone (10 ml.), leaving a residue (0·2 g.) which contained antimony and had m. p. >330°, but was not further identified. The fraction soluble in acetone, after crystallisation from benzene, had m. p. 190—190·5° and was almost certainly 4-diphenylyloxyacetic acid (m. p. 189—190°) [9] (Found: C, 72·9; H, 5·4. Calc. for $C_{14}H_{12}O_3$: C, 73·7; H, 5·3%).

Stibiafluorene Dibromides (IV).—The stibiafluorene (0·5 g.) was dissolved in the minimum of carbon tetrachloride, cooled to 0°, and the calculated quantity of bromine added from a micropipette. The dibromide separated almost immediately (0·4—0·5 g.) and was recrystallised from carbon tetrachloride. The *dibromide* (IV; R = H, R′ = CO_2H, R″ = Me) had m. p. 195° (decomp.) (Found: C, 34·4; H, 2·1. $C_{20}H_{15}O_2Br_2Sb,CCl_4$ requires C, 34·9; H, 2·1%); (IV; R = Br, R′ = H, R″ = Me) had m. p. 190°, with slight previous shrinkage (Found: C, 31·6; H, 2·2; Sb, 16·1. $C_{19}H_{14}Br_2Sb,CCl_4$ requires C, 31·7; H, 1·9; Sb, 16·1%); and (IV; R = Br, R′ = H, R″ = CO_2Et) had m. p. 188—189° again with previous shrinkage but no obvious decomposition (Found: C, 32·8; H, 2·0; Sb, 15·0. $C_{21}H_{16}O_2Br_2Sb,CCl_4$ requires C, 32·4; H, 2·0; Sb, 14·9%). Analysis of these compounds by the modified Stepanow method [10] gave weights of mixed silver halide representing only 70—90% of the calculated total, presumably because some loss of carbon tetrachloride occurred during decomposition. The *ester dibromide* (IV; R = Br, R′ = H, R″ = CO_2Et) was recrystallised thrice from benzene and then had m. p. 194—195° (Found: C, 40·0; H, 2·7. $C_{21}H_{16}O_2Br_2Sb,\frac{1}{2}C_6H_6$ requires C, 40·2; H, 2·6%). The same product was isolated directly when bromination was carried out in benzene.

[9] Clark, "Semi-micro Quantitative Organic Analysis," Academic Press, 1943, p. 53.
[10] *Chem. Abs.*, 1946, **40**, 1474.

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Hydrated Stibiafluorene Oxides.—The dibromide (0·2—0·5 g.) was dissolved in 10% alcoholic sodium hydroxide (5 ml.) and warmed to 60° for 10 min., and the product isolated by acidification. In the case of (IV; R = H, R′ = CO_2H, R″ = Me) the gelatinous precipitate obtained was purified by dissolution in aqueous sodium hydrogen carbonate and reprecipitation, and when dried *in vacuo* at 100° had m. p. >310° (Found: C, 44·4, 43·8; H, 3·5, 3·8. $C_{20}H_{17}O_4Sb$ requires C, 54·2; H, 3·9%). The product from (IV; R = Br, R′ = H, R″ = Me), after recrystallisation from ethyl acetate–ethanol, had m. p. 275—280° (Found: C, 46·1; H, 3·9. $C_{19}H_{16}O_2BrSb,H_2O$ requires C, 46·0; H, 3·7%), and that from (IV; R = Br, R′ = H, R″ = CO_2Et) had m. p. 302—304° (Found: C, 45·2; H, 3·4. $C_{21}H_{18}O_4BrSb,H_2O$ requires C, 45·5; H, 3·6%).

Attempted Oxidation by Hydrogen Peroxide.—2-Carboxy-9-*p*-tolyl-9-stibiafluorene (0·1 g.) was dissolved in glacial acetic acid (3 ml.), and then hydrogen peroxide (100-vol.; 1 ml.) was added at room temperature. The precipitate which separated immediately was filtered off after 30 min. and when dried at 100° (vac.) had m. p. >310° (Found: C, 49·2; H, 3·4%). When this experiment was repeated with the (−)-isomer, $[\alpha]_D$ −245·7° (*c* 0·25 in pyridine), the precipitate obtained had m. p. >310°, $[\alpha]_D$ = 0° (*c* 0·285 in pyridine; *l* = 2).

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THE UNIVERSITY, SOUTHAMPTON. [*Received, December 1st,* 1958.]

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289. *Electrolytic Conductance of Solutions of Halogenotrifluoromethylphosphoranes.*

By H. J. EMÉLEUS and G. S. HARRIS.

Dichlorotristrifluoromethylphosphorane, $PCl_2(CF_3)_3$, is a conductor, and trichlorobistrifluoromethylphosphorane, $PCl_3(CF_3)_2$, a non-conductor, in acetonitrile. Values of molar conductance are given. The infrared spectra of the vapours of the two phosphoranes are recorded. Conductometric titration of tristrifluoromethylphosphine $P(CF_3)_3$ with bromine in acetonitrile provides evidence for the existence of an ionic compound of composition $P(CF_3)_3,Br_2$.

MANY derivatives of phosphine readily add a halogen molecule to produce, formally at least, a compound in which a phosphorus(v) atom is attached by covalent bonds to five univalent atoms or groups: $PX_3 + Y_2 \longrightarrow PX_3Y_2$. When these groups about the phosphorus atom are electron-attracting, the adduct may, under certain conditions, display well-defined ionic properties. An example of this dual behaviour is afforded by phosphorus pentachloride, which exists as trigonal bipyramidal molecules in the vapour phase [1] and as ions, PCl_4^+ PCl_6^-, in the solid state; [2] the same ions are also present in solutions in solvents of high dielectric constant.[3] When X is an electronegative organic group (*e.g.*, phenoxy-), the adduct containing quinquevalent phosphorus may also undergo ionic dissociation. For example, the following equilibria occur in acetonitrile: [4]

$$2P(OPh)_3 + 2Br_2 \rightleftharpoons 2P(OPh)_3Br_2 \rightleftharpoons P(OPh)_3Br^+ + P(OPh)_3Br_3^-$$

Compounds of the general type PX_nY_{5-n} in which X is the trifluoromethyl group have recently been prepared.[5,6] Account being taken of the strongly electronegative character of the trifluoromethyl group, and its pseudo-halogenoid behaviour in certain derivatives,[5] it was of interest to study the halogenotrifluoromethylphosphoranes more fully to find out if their properties followed the general pattern outlined above for phosphorus(v)

[1] Rouault, *Compt. rend.*, 1938, **207**, 620.
[2] Clark, Powell, and Wells, *J.*, 1942, 642.
[3] Payne, *J.*, 1953, 1052.
[4] Harris and Payne, *J.*, 1956, 3038.
[5] Bennett, Emeléus, and Haszeldine, *J.*, 1953, 1565.
[6] Emeléus, Haszeldine, and Ram Chand Paul, *J.*, 1955, 563.

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halides and related compounds. We now report an investigation of the properties of halogenotrifluoromethylphosphoranes of the types $P(CF_3)_3Hal_2$ and $P(CF_3)_2Hal_3$.

Dichlorotristrifluoromethylphosphorane, which at room temperature is a colourless solid, dissolves readily in acetonitrile, a solvent that has been widely used as an ionising medium for non-metallic halides and polyhalides.[7,8] Measurement of the conductance of the solutions immediately after their preparation gave a very low value (*ca.* 1×10^{-5} ohm^{-1} cm.$^{-1}$) for their specific conductance, but on standing, the conductance increased gradually and after 48 hr. a steady high value (*ca.* 3×10^{-3} ohm^{-1} cm.$^{-1}$) was observed. Solutions covering a range of concentration were examined and the values of " steady " molar conductance obtained are given in the table below. When molar conductance is

Conductance of dichlorotristrifluoromethylphosphorane in acetonitrile at 15°.

c_m (mole l.$^{-1}$)	0·0248	0·0375	0·0515	0·0704	0·1492	0·2313
$10^4\kappa$ (ohm^{-1} cm.$^{-1}$)	12·19	16·46	21·41	27·17	27·00	29·64
Λ_m (ohm^{-1} cm.^{2} mole^{-1})	49·2	43·9	41·6	38·6	18·1	12·8

plotted against the square root of the molar concentration the points fall nearly on a straight line which, on extrapolation to zero concentration, gives a value of 66 ohm^{-1} cm.^{2} mole^{-1} for the molar conductance at infinite dilution ($\Lambda_{m,\infty}$). This is a significantly high figure, being greater than that for acetonitrile solutions of phosphorus pentabromide ($\Lambda_{m,\infty} = 20$ ohm^{-1} cm.^{2} mole^{-1}) [8] and pentachloride ($\Lambda_{m,\infty} = 35$ ohm^{-1} cm.^{2} mole^{-1}),[9] and less than that for solutions of dichlorotriphenoxyphosphorane ($\Lambda_{m,\infty} = 105$ ohm^{-1} cm.^{2} mole^{-1}).[4] Thus the high conductance of these solutions leads to the conclusion that in acetonitrile, dichlorotristrifluoromethylphosphorane ionises with the probable occurrence of solvation of the ions. The mode of ionisation has not been determined directly, but by analogy with phosphorus pentachloride and pentabromide,[3,8] and dibromotriphenoxyphosphorane,[4] the ionisation occurring in the solution may be of the overall form,

$$2P(CF_3)_3Cl_2 \rightleftharpoons P(CF_3)_3Cl^+ + P(CF_3)_3Cl_3^-$$

In solution, molecular equilibrium of the type,

$$P(CF_3)_3Cl_2 \rightleftharpoons P(CF_3)_3 + Cl_2$$

cannot be excluded, but the products of such a dissociation could not account for the high value of conductance since tristrifluoromethylphosphine and halogens are non-conductors in acetonitrile.

Conductometric titration of an acetonitrile solution of dichlorotristrifluoromethylphosphorane with an acetonitrile solution of water resulted in a steep drop in specific conductance from $1{\cdot}3 \times 10^{-3}$ to $2{\cdot}5 \times 10^{-5}$ ohm^{-1} cm.$^{-1}$ at mole ratio 1 : 1. Thereafter the conductance rose very slowly as further volumes of the aqueous acetonitrile were added. This result is in accord with the accepted mode of hydrolysis of dichlorotristrifluoromethylphosphorane:

$$P(CF_3)_3Cl_2 + H_2O \rightleftharpoons P(CF_3)_3O + 2HCl$$

and precludes the possibility that the high values of the conductance of the phosphorane solutions are due to traces of moisture in the measuring system. The stability of acetonitrile as a solvent for $PCl_2(CF_3)_3$ has been demonstrated by recovery of the solute after 24 hours' standing.

The variation of conductance with time is an interesting but not unique feature of this system. A similar drift in conductance has been observed by Popov and Deskin [10] in acetonitrile solutions of iodine halides, where the effect is thought to be due to a slow

[7] Popov and Skelly, *J. Amer. Chem. Soc.*, 1954, **76**, 5309.
[8] Harris and Payne, *J.*, 1956, 4617.
[9] *Idem*, unpublished results.
[10] Popov and Deskin, *J. Amer. Chem. Soc.*, 1958, **80**, 2976.

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conversion of the solvated covalent molecule into a solvated ion-pair: $CH_3{\cdot}CN,IX \longrightarrow CH_3{\cdot}CNI^+X^-$. The "slow ionisation" of dichlorotristrifluoromethylphosphorane may be due to a similar type of process in which a change from a covalent molecule to an ion-pair occurs, and it has been shown that dichlorotrifluorophosphorane (PF_3Cl_2) behaves in much the same way.[11]

The conductance of trichlorobistrifluoromethylphosphorane in acetonitrile was studied under the same conditions as applied to dichlorotristrifluoromethylphosphorane. In this case, however, the values of conductance were about fifty times lower ($\Lambda_{m,\infty} < 1$). This compound must therefore, in relation to the other PX_nHal_{5-n} derivatives so far discussed, be regarded as a non-conductor in acetonitrile.

The difference in behaviour of the two phosphoranes under discussion, when dissolved in an ionising medium, may possibly be connected with differences between the structures of the covalent molecules. Although a direct structural determination has not been carried out, the molecule of trichlorobistrifluoromethylphosphorane appears, from the absorption in the carbon–fluorine stretching region of its infrared spectrum, to have the symmetrical trigonal bipyramidal structure in which the apices are occupied by the trifluoromethyl groups. It has also been postulated that ionisation of phosphorus pentahalides in a suitable environment occurs through a mechanism involving ionisation of the apical bond.[12,13] This, together with the fact that the CF_3^- ion has not been observed in any system, appears to explain the non-ionic behaviour of trichlorobistrifluoromethylphosphorane. The infrared spectrum of the dichloro-analogue does not lead to the assignment of a definite structure to the compound. It seems probable that there is present a mixture of configurations, at least one of which contains an apical phosphorus–chlorine bond which is the site of ionisation.

Attempts to prepare dibromotristrifluoromethylphosphorane were not successful. However, there is evidence to suggest that in acetonitrile an ionic compound of composition $P(CF_3)_3,Br_2$ does exist, since the stepwise addition of bromine to an acetonitrile solution of $P(CF_3)_3$ causes the conductance of the latter to increase steadily until the mole ratio 1 : 1 is reached: thereafter, the conductance of the solution rises only slowly. This behaviour resembles closely that of the system phosphorus tribromide–bromine (leading to PBr_5),[8] but at the 1 : 1 ratio the molar conductance is higher ($\Lambda_m = 9{\cdot}75$ ohm^{-1} cm.^{2} mole^{-1} at molar concentration 0·20; PBr_5, $\Lambda_m = 1{\cdot}0$ at molar concentration 0·20 [9]).

Experimental

The trifluoromethylphosphorus compounds were prepared from the autoclave reaction of red phosphorus and trifluoroiodomethane.[5,14] This yielded, after separation by fractionation *in vacuo* and fractional distillation, tristrifluoromethylphosphine, iodobistrifluoromethylphosphine, and di-iodotrifluoromethylphosphine. The last two compounds were converted into the more stable chloro-derivatives by reaction with silver chloride. The compounds were handled in a vacuum system and a nitrogen-filled dry-box.

Dichlorotristrifluoromethylphosphorane and trichlorobistrifluoromethylphosphorane were prepared by addition of 1 mole of chlorine to 1 mole of tristrifluoromethylphosphine and 1 mole of chlorobistrifluoromethylphosphine, respectively.[5,6] A modified method of purification was here employed to yield analytically pure materials. This involved fractionation *in vacuo*, through suitably cooled traps. Since both of the phosphoranes have an appreciable vapour pressure at room temperature they may be handled conveniently in a vacuum system. The m. p.s were measured *in vacuo* in a Stock-type plunger apparatus: $P(CF_3)_3Cl_2$, m. p. 24·0—25·5° (previous value, 20·5° [5]); $P(CF_3)_2Cl_3$, m. p. −26·0° to −25·0° Extrapolation of the vapour-pressure curve for dichlorotristrifluoromethylphosphorane gave b. p. 107°, compared with the earlier value of 94°. Pure anhydrous acetonitrile suitable for the conductance experiments

[11] Kennedy and Payne, *J.*, in the press.
[12] Siebert, *Z. anorg. Chem.*, 1951, **265**, 303.
[13] Kolditz, *ibid.*, 1957, **293**, 147.
[14] Bennett, Brandt, Emeléus, and Haszeldine, *Nature*, 1950, **166**, 225.

was prepared by Smith and Witten's method.[15] The purified product had κ 10^{-7} ohm^{-1} cm.$^{-1}$ at 25°.

Conductance Experiments.—For these measurements, use was made of a small dipping-electrode type of cell which was adapted to enable the introduction of solute and solvent by distillation *in vacuo*. The electrodes were of smooth platinum and the cell constant was 0·8233 cm.$^{-1}$ (electrodes *ca.* 1 cm. apart; minimum capacity, 2 ml. of solution). Values of conductance were measured by using the Wheatstone bridge apparatus described by Haszeldine and Woolf,[16] or, in cases where a portable bridge was more suitable, a Mullard Conductance Bridge Type E7566. The conductance cell was placed in a thermostat below room temperature, since throughout the experiment the cell was kept evacuated.

Conductometric Titration.—The same conductance cell was used for this experiment and contained the acetonitrile solution of tristrifluoromethylphosphine to be titrated. Successive additions of known weights of the titrant (bromine) were added to the cell by distillation *in vacuo*, and the conductance was measured when equilibrium had been attained following each addition of bromine. This experiment was performed at room temperature.

Infrared Spectra.—The spectra were studied in the region 4000—400 cm.$^{-1}$ by use of a Perkin-Elmer Model 21 double-beam spectrometer fitted with sodium chloride and potassium bromide prisms. The compounds were examined as vapours in a 10 cm. cell with sodium chloride or potassium bromide windows. Values of frequencies of absorption and a qualitative estimate of their intensity are as follows:

$P(CF_3)_3Cl_2$, 2285w, 2250w, 1327m, 1280m, 1227vs, 1201vs, 1186vs, 1148vs, 1133vs, 1096vs, 756m, 596s, 527s, 502s.

$P(CF_3)_2Cl_3$, 2280w, 1326w, 1273m, 1262m, 1226m, 1182vs, 1147vs, 1017w, 790w, 741w, 690w, 613w, 585vs, 529vs.

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[*Received, December 17th*, 1958.]

[15] Smith and Witten, *Trans. Faraday Soc.*, 1951, **47**, 1304.
[16] Haszeldine and Woolf, *Chem. and Ind.*, 1950, 544.

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290. *The Formation of Halogenoperfluoroalkylmercurates.*[1]

By H. J. Emeléus and J. J. Lagowski.

Conductometric titrations of perfluoroalkylmercury compounds with potassium halides and ammonium thiocyanate indicate the formation of halogenoperfluoroalkylmercurate(II) anions in aqueous solution. Addition of solutions containing the 5 : 6-benzoquinolinium ion or the ethylenediamine complexes of zinc(II), copper(II), cadmium(II), or nickel(II) to mixed solutions of alkali iodides and bis(trifluoromethyl)mercury, trifluoromethylmercuric iodide, or heptafluoro-*n*-propylmercuric iodide precipitates salts containing the anions $[Hg(CF_3)I_3]^{2-}$, $[Hg(CF_3)_2I_2]^{2-}$, or $[Hg(C_3F_7)I_3]^{2-}$.

The existence of anions containing the trifluoromethyl group has been established in the trifluoromethylantimonic acid series,[2] and the experiments described below were made to determine if analogous halogenoperfluoroalkylmercurate(II) anions are also stable. Such anions would be derivatives of tetrahalogenomercurate(II) ions, which are well known, and for which the stability decreases in the order iodo- > bromo- > chloro-. The ion $(HgF_4)^{2-}$ is known but is hydrolysed by water. It was found in preliminary experiments that the *X*-ray diffraction pattern of the residue on evaporation of an aqueous solution of a potassium halide and bis(trifluoromethyl)mercury, or heptafluoro-*n*-propylmercuric

[1] For a preliminary account of this work, see Emeléus and Lagowski, *Proc. Chem. Soc.*, 1958, 231.
[2] Emeléus and Moss, *Z. anorg. Chem.*, 1955, **282**, 24.

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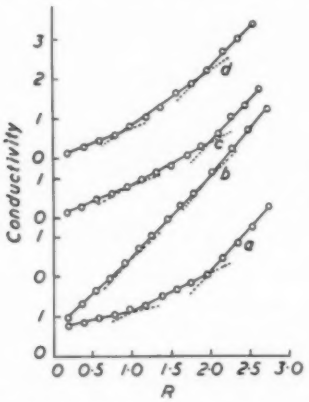
iodide, in a 1 : 1 or 2 : 1 molar ratio did not contain lines characteristic of the reactants. With a ratio 3KI : $Hg(CF_3)_2$, the characteristic lines of potassium halide were observed, but none of those of the mercurial. Moreover, whereas heptafluoro-*n*-propylmercuric iodide was very sparingly soluble in water, it dissolved readily in presence of halide ions. These observations led to an examination of the formation of halogenoperfluoroalkylmercurate(II) ions by conductometric titration. Typical results are shown in the Figure for titration of aqueous solutions of bis(trifluoromethyl)mercury with potassium (*a*) chloride, (*b*) thiocyanate, (*c*) iodide, and (*d*) bromide. The abscissæ are all on the same scale but are adjusted vertically for clarity. The mercurial itself has a small conductivity,[3] and this is increased by addition of halide, though by less than would arise from the halide alone. Breaks are expected to accompany the formation of new ionic species only if there are relatively large changes in ionic mobility and also in thermodynamic stability. The evidence afforded by the titration results is not, therefore, decisive but must be considered in conjunction with the preparative work described later which has led to the isolation of compounds containing some of the ions postulated.

The results for the three halides in the Figure could be fitted to smooth curves but, the preparative work being borne in mind, it is justifiable to represent them as falling on



Plot of conductivity × 10^3 (*ohm*$^{-1}$ *cm.*$^{-1}$) *against R, the ratio of halide to* $Hg(CF_3)_2$ *concentration* (*mole l.*$^{-1}$).

straight lines which intersect in each case at halide : mercurial ratios of 1 : 1 and 1 : 2, indicating the formation of the new ionic species $[Hg(CF_3)_2X]^-$ and $[Hg(CF_3)_2X_2]^{2-}$. No compounds containing ions of the first type have been prepared, though two were made which contained $[Hg(CF_3)_2I_2]^{2-}$ (see Table). The results of the titration with ammonium thiocyanate (Fig., *b*) were inconclusive since no breaks were found.

In the titration of trifluoromethylmercuric bromide with the same halides there were breaks at 1 : 1 and 1 : 2 for potassium iodide and at 1 : 2 for the bromide, but no breaks were observed with potassium chloride. The formation of $[Hg(CF_3)BrI]^-$, $[Hg(CF_3)BrI_2]^{2-}$, and $[Hg(CF_3)Br_3]^{2-}$ may be deduced, but it is probable that $[Hg(CF_3)Br_2]^-$, $[Hg(CF_3)BrCl]^-$, and $[Hg(CF_3)BrCl_2]^{2-}$ are unstable. In the titration of trifluoromethylmercuric iodide with potassium chloride, bromide, and iodide there are in each case breaks at halide : mercurial ratios of 1 : 1 and 1 : 2, indicating the formation in solution of the ionic species $[Hg(CF_3)IX]^-$ and $[Hg(CF_3)IX_2]^{2-}$ (X = Cl, Br, or I), and several derivatives containing the ion $[Hg(CF_3)I_3]^{2-}$ were isolated (Table). There were no clear breaks in the titration curves for ammonium thiocyanate in this case. With heptafluoro-*n*-propylmercuric iodide breaks occurred at 1 : 1 and 2 : 1 ratios with potassium iodide and bromide, and with potassium chloride there was an ill-defined break at a 1 : 2 ratio. These results can be interpreted in the same way, those for the potassium iodide titration being supported by

[3] Emeléus and Haszeldine, *J.*, 1949, 2948, 2953.

the preparation of a compound containing $[Hg(C_3F_7)I_3]^{2-}$. It seems from this evidence that the anions become less stable in passing from the iodo- to the chloro-type.

Anionic complexes of mercury containing organic radicals, other than cyanide, have not been previously reported, although compounds of the type $LiMPh_3$ have been characterised for the other elements of Group IIB.[4] Their relative stabilities are in the order $LiZnPh_3 > LiCdPh_3 > LiPh + HgPh_2$ (no compound formed). The nature of these compounds is unknown, but the order of stability is the reverse of that of the tetrahalogenometallate ions. Only zinc alkyls react with alkyls of the alkali or the alkaline-earth metals to form compounds containing tetra-alkylmetallate ions[5] and, though perfluoroalkyl derivatives of zinc[6] and cadmium[7] have been described, no derived complexes, other than solvates of the zinc compounds, are known.

The interpretation of the results of conductometric titrations is supported by the preparation of compounds containing halogenoperfluoroalkylmercurate ions. Salts of ethylenediamine–transition metal complexes were chosen as precipitating reagents because they give insoluble compounds with tetrahalogenomercurate anions. The compounds containing tris(ethylenediamine)zinc(II) or bis(ethylenediamine)cadmium(II) were white, those with tris(ethylenediamine)nickel(II) violet, and those with bis(ethylenediamine)-copper(II) dark purple. All resembled the corresponding compounds containing the tetrahalogenomercurate anions. The insoluble compounds isolated contained $[Hg(CF_3)I_3]^{2-}$, $[Hg(C_3F_7)I_3]^{2-}$, or $[Hg(CF_3)_2I_2]^{2-}$ (see Table). Attempts to isolate bromo- and chloro-perfluoroalkylmercurate derivatives of the cations examined were unsuccessful, although tetraphenylarsonium chloride, when added to an aqueous solution of bis(trifluoromethyl)mercury containing chloride ions, gave an immediate white precipitate which gave trifluoromethane on alkaline hydrolysis. This preliminary result indicates that derivatives of other anions could probably be isolated by a suitable choice of cation, but the relative stabilities of anions cannot be deduced from the ease of isolation of these derivatives. Aqueous solutions of trifluoromethylmercuric iodide containing potassium iodide lose trifluoromethane forming a yellow solution which presumably contains tetra-iodomercurate ions.[1] A similar decomposition may have occurred in the attempted preparation of bis(ethylenediamine)cadmium(II) di-iodobis(trifluoromethyl)mercurate(II), the product from which contained too high a proportion of iodine. The decomposition in presence of iodide ion probably occurs as follows:

$$Hg(CF_3)_2I_2^{2-} + I^- + H_2O \longrightarrow Hg(CF_3)I_3^{2-} + CHF_3 + OH^-$$

$$Hg(CF_3)I_3^{2-} + I^- + H_2O \longrightarrow HgI_4^{2-} + CHF_3 + OH^-$$

Tris(ethylenediamine)zinc(II) di-iodobis(trifluoromethyl)mercurate(II) and tris(ethylenediamine)nickel(II) di-iodobis(trifluoromethyl)mercurate(II) dissolve in hot water or hot aqueous potassium iodide solutions and liberate trifluoromethane quantitatively. Cations which would not form precipitates with di-iodobis(trifluoromethyl)mercurate anions readily did so in 70—80% yield with tri-iodo(trifluoromethyl)mercurate(II) ions. Tris(ethylenediamine)zinc(II), bis(ethylenediamine)copper(II), tris(ethylenediamine)-nickel(II), bis(ethylenediamine)cadmium(II), and di-(5 : 6-benzoquinolinium) tri-iodo(trifluoromethyl)mercurate(II) were soluble, with reaction, in hot water, and trifluoromethane was formed quantitatively. In decomposing these compounds for analysis it was found that the $Hg–C_3F_7$ bond was less readily broken than $Hg–CF_3$. An attempt to isolate silver tri-iodoheptafluoro-*n*-propylmercurate(II) by the addition of silver nitrate to a solution of heptafluoro-*n*-propylmercuric iodide containing potassium iodide (all substances in stoicheiometric amounts) was unsuccessful: there was an immediate precipitate of silver iodide which was identified by its *X*-ray pattern.

[4] Wittig and Hornberger, *Annalen*, 1952, **557**, 11.
[5] Hurd, *J. Org. Chem.*, 1948, **13**, 711; Gilman, Meals, O'Donnell, and Woods, *J. Amer. Chem. Soc.*, 1943, **65**, 268; Gilman and Woods, *ibid.*, 1945, **67**, 520.
[6] Haszeldine and Walaschewski, *J.*, 1953, 3607; Miller, Bergman, and Fainberg, *J. Amer. Chem. Soc.*, 1957, **79**, 4159.
[7] Haszeldine, *Nature*, 1951, **168**, 1028.

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Experimental

Trifluoromethylmercuric iodide, m. p. 112°, was prepared by irradiating trifluoroiodomethane with mercury and was then converted into trifluoromethylmercuric bromide, m. p. 83°. Bis(trifluoromethyl)mercury was prepared from trifluoroiodomethane and cadmium amalgam.[3] Mercury (10 ml.) was sealed with heptafluoroiodopropane [7] in an evacuated tube and heated at 220° for 24 hr. in a rocking furnace. The white crystalline product was extracted with ether and gave *heptafluoro*-n-*propylmercuric iodide* (10·4 g.) which was sublimed at 80° in nitrogen to lustrous white plates, m. p. 77·0—77·5° (Found: C_3F_7, 34·1; I, 25·2%. C_3F_7IHg requires C_3F_7, 34·0; I, 25·6%), soluble in common organic solvents but not in water. Heptafluoroiodopropane (4·89 g.) was recovered.

Conductivities were measured at 20° in a cell of 5 ml. capacity, closed by a rubber serum cap, through which the potassium halide solution was added with a calibrated Agla micrometer syringe. About 4 ml. of mercurial solution of known concentration were used, the cell being shaken after each addition of titrant. Measurements were made with an A.C. bridge with a visual null-point indicator.[8] Since the volume of titrant was not negligible compared with the volume of mercurial solution, the resistance measurements were corrected for dilution. All solutions were prepared in distilled water except those of heptafluoro-*n*-propylmercuric iodide, which was dissolved in aqueous methanol (1 : 1 w/w). All the mercurials were resublimed immediately before use. Samples for *X*-ray examination were prepared by dissolving stoicheiometric mixtures of potassium halide and bis(trifluoromethyl)mercury or heptafluoro-*n*-propylmercuric iodide in acetone, with the addition of a little water in the case of potassium chloride and bromide. The solvent was evaporated in a vacuum at room temperature, and the samples were handled subsequently in a dry-box in nitrogen.

The same general procedure was used in preparing all the compounds containing the halogenoperfluoroalkylmercurate ions: details are given for the typical preparation of tris(ethylenediamine)zinc(II) tri-iodo(trifluoromethyl)mercurate(II). Analytical data for the remaining compounds are given in the Table.

	Found (%)	Reqd. (%)
$Cu(C_2H_8N_2)_3HgCF_3I_3$		
I	45·1	45·6
Hg	24·7	24·1
Cu	7·28	7·63
CF_3	8·15	8·29
$Ni(C_2H_8N_2)_3HgCF_3I_3$		
I	42·3	42·85
Hg	22·3	22·5
Ni	6·38	6·61
CF_3	7·35	7·77
N	10·0	9·47
$Cd(C_2H_8N_2)_2HgCF_3I_3$		
I	42·95	43·1
Hg	22·6	22·7
Cd	12·5	12·7
CF_3	7·50	7·81
$(C_{12}H_9NH)_2HgCF_3I_3$		
I	37·9	37·6
Hg	19·8	19·9
CF_3	6·66	6·80
N	3·08	2·78
$Zn(C_2H_8N_2)_3HgC_3F_7I_3$		
I	38·5	38·2
Zn	7·10	6·55
C_3F_7	16·6	17·0
N	8·65	8·43
$Zn(C_2H_8N_2)_3Hg(CF_3)_2I_2$		
I	30·4	30·3
Hg	23·4	23·95
Zn	7·91	7·97
CF_3	16·0	16·5
$Ni(C_2H_8N_2)_3Hg(CF_3)_2I_2$		
I	30·6	30·45
CF_3	16·1	16·6
N	9·77	10·0

Preparation of Tris(ethylenediamine)zinc(II) *Tri-iodo(trifluoromethyl)mercurate*(II).—To 2M-aqueous potassium iodide (10 ml.) was added trifluoromethylmercuric iodide (0·105 g.) followed by a two-fold excess of tris(ethylenediamine)zinc(II) sulphate, prepared by dissolving the required amount of zinc sulphate in 1M-potassium iodide and adding excess of ethylenediamine. A fine white granular precipitate formed immediately and was filtered on a sintered crucible, washed with cold water, ethanol, and ether, and kept in an evacuated desiccator for 30 min. The dry product weighed 0·195 g. (82% yield on trifluoromethylmercuric iodide) [Found: I, 43·0; Zn, 7·56; CF_3, 7·40%. $Zn(C_2H_8N_2)_3HgCF_3I_3$ requires I, 42·5; Zn, 7·30; CF_3, 7·60%].

In an attempt to prepare bis(ethylenediamine)cadmium(II) di-iodobis(trifluoromethyl)mercurate(II), a solution prepared from 2M-potassium iodide (20 ml.) and bis(trifluoromethyl)mercury was mixed with excess of a solution of bis(ethylenediamine)cadmium(II) sulphate. A white solid (0·0956 g.) formed after 4 hr. [Found: I, 45·8; CF_3, 2·20%. Calc. for

[8] Haszeldine and Woolf, *Chem. and Ind.*, 1950, 544.

$Cd(C_5H_5N)_2Hg(CF_3)_2I_2$: I, 30·75; CF_3, 16·7%. Calc. for $Cd(C_5H_5N)_2HgCF_3I_2$: I, 43·9; CF_3, 7·77%. Calc. for $Cd(C_5H_5N)_2HgI_4$: I, 53·85%]. Similar analytical results were obtained in attempts to prepare bis(ethylenediamine)copper(II) di-iodobis(trifluoromethyl)mercurate(II) and di-(5 : 6-benzoquinolinium) di-iodobis(trifluoromethyl)mercurate(II).

Trifluoromethyl and heptafluoropropyl groups were estimated by heating in a sealed tube at 100° for 4 hr. with 15% sodium hydroxide and measuring the CHF_3 or C_3F_7H produced. Zinc was determined as zinc–2-methylquinoline monohydrate,[9] cadmium as cadmium–dipyridine thiocyanate,[10a] nickel as either nickel sulphide or nickel–dipyridine thiocyanate,[10b] copper as bis(ethylenediamine)copper(II) tetraiodomercurate(II), and mercury as mercuric sulphide or bis(ethylenediamine)copper(II) tetraiodomercurate(II).[10c] Compounds containing the di-iodobis(trifluoromethyl)mercurate(II) or tri-iodotrifluoromethylmercurate(II) anion were decomposed for analysis by hot dilute acetic acid. Compounds containing the $Hg–C_3F_7$ bond were decomposed by hot alcoholic potassium hydroxide. Infrared spectra were recorded as Nujol mulls.

One of us (J. J. L.) acknowledges a Marshall Scholarship.

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[9] Flagg, "Organic Reagents Used in Gravimetric and Volumetric Analysis," Interscience Publishers Inc., New York, 1948, 255.
[10] Vogel, "Quantitative Inorganic Analysis," Longmans, Green and Co., London, 1951, (*a*) p. 429, (*b*) p. 458, (*c*) p. 433.

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291. *Carbonyl Halides of Manganese and Some Related Compounds.*

By E. W. ABEL and G. WILKINSON.

Thermal decomposition of the corresponding pentacarbonyl halide has produced the three bridged manganese tetracarbonyl halides $[Mn(CO)_4X]_2$ (X = Cl, Br, and I). A number of disubstitution products $L_2M(CO)_3X$ (L = C_5H_5N, Ph_3P, and Ph_3As; L_2 = dipy) have been prepared. The carbonyl stretching frequencies in the infrared spectra of the compounds are recorded.

SINCE the discovery of manganese carbonyl, and its treatment with iodine at 140° to produce [1] the pentacarbonyl iodide, other manganese carbonyl halides have been prepared. Except for the infrared spectra of the bromide [2] and iodide,[1] no properties of these compounds have been given, although the chloride [2,3] and bromide [4] have been mentioned.

Manganese pentacarbonyl chloride and bromide have been made by the action of the halogen on a solution of manganese carbonyl at a lower temperature than that required [1] for the iodide. Bromine reacted rapidly with the carbonyl at 40°, and chlorine at 0°. Higher temperatures led to almost complete decomposition to manganese halides. The pentacarbonyl halides were purified either by vacuum sublimation or by recrystallisation from light petroleum.

Thermal decomposition of the manganese pentacarbonyl chloride, bromide, and iodide produced the corresponding tetracarbonyl halides:

$$2Mn(CO)_5X \longrightarrow [Mn(CO)_4X]_2 + 2CO \quad \ldots\ldots\ldots (I)$$

The reaction is best carried out in an inert solvent at 120°, but in contrast to the very good yields of the tetracarbonyl halides of rhenium formed [5] in this way, the yields are low (*ca.* 40%) owing to the concurrent decomposition and formation of manganese halides.

Molecular-weight measurements of these tetracarbonyl halides of manganese have

[1] Brimm, Lynch, and Sesny, *J. Amer. Chem. Soc.*, 1954, **76**, 3831.
[2] Wilson, *Z. Naturforsch.*, 1958, **13**b, 349.
[3] Hieber and Wagner, *Z. Naturforsch.*, 1958, **13**b, 339.
[4] Coffield, Kozikowski, and Closson, *J. Org. Chem.*, 1957, **22**, 598.
[5] Abel, Hargreaves, and Wilkinson, *J.*, 1958, 3149.

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shown them to be dimeric, and analogous to the corresponding [5] rhenium compounds. In both the pentacarbonyl and the tetracarbonyl halides of manganese there is a gradual darkening in colour from chloride to iodide (Table 1). The dimeric carbonyl halides are considerably less soluble in organic solvents than the monomeric pentacarbonyl halides, but are more soluble than the corresponding rhenium compounds, and can be recrystallised readily from benzene. Also, unlike their rhenium analogues, the manganese tetracarbonyl halides can be sublimed *in vacuo*, in each case at a temperature about 70° higher than for the corresponding monomeric pentacarbonyl halide.

TABLE 1. *Carbonyl halides of manganese.*

Compound	Colour	CO stretching modes ($cm.^{-1}$) *	Compound	Colour	CO stretching modes ($cm.^{-1}$) *
$Mn(CO)_5Cl$	Pale yellow	2070, 2016	$[Mn(CO)_4Cl]_2$	Orange	2061, 2023, 1982, 1952
$Mn(CO)_5Br$	Yellow	2064, 2017	$[Mn(CO)_4Br]_2$	Brown	2056, 2023, 1982, 1954 (sh.)
$Mn(CO)_5I$	Orange	2056, 2017	$[Mn(CO)_4I]_2$	Dark brown	2048, 2022, 1983

* All strong unless otherwise noted.

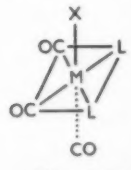
The infrared spectra of the manganese tetracarbonyl halides in the 1700—2200 $cm.^{-1}$ region are similar to those of the rhenium analogues,[5] and the structure is undoubtedly the same as that of the rhenium compounds, with a halogen bridge, as in a number of other carbonyl halide structures. The manganese tetracarbonyl halides reacted with carbon monoxide under high temperature and pressure to form the pentacarbonyl halides, thus showing reaction (1) to be reversible depending upon conditions.

A few substituted rhenium carbonyl halides have previously been prepared [6,7] by the interaction of the rhenium pentacarbonyl halides with certain ligands, and we have already mentioned [5] the formation of bispyridinerhenium tricarbonyl iodide from the dimeric tetracarbonyl halide. We have now prepared (Table 2) a number of substitution products of the rhenium and manganese carbonyl halides in which nitrogen, phosphorus, and arsenic act as donor atoms. These compounds have been prepared by the direct action of the ligand, with either the metal pentacarbonyl halide (method A) or the tetracarbonyl halide (method B), or in some cases both, to show the identity of the product:

$$M(CO)_5X + 2L \longrightarrow L_2M(CO)_3X + 2CO \quad . . . . . (2)$$

$$[M(CO)_4X]_2 + 4L \longrightarrow 2L_2M(CO)_3X + 2CO \quad . . . . . (3)$$

In every case the reaction was notably faster for the tetracarbonyl halide, owing to the bridging structure's providing a reactive centre in the molecule. We believe all these compounds have the general structure (inset), in which the two ligands are introduced into the carbonyl compound in the *cis*-position to each other, from arguments already cited.[5] This view is now further supported by the preparation of the 2 : 2′-dipyridyl compounds, in which the infrared spectra of the carbonyl stretching region are very similar to those of the corresponding bispyridine compounds.



The compound $[(Ph_3P)_2Re(CO)_4]^+Cl^-$ has been reported [7] to be formed by reaction between triphenylphosphine and rhenium pentacarbonyl chloride. The substitution product which we have prepared from these reagents we regard to be $(Ph_3P)_2Re(CO)_3Cl$ on the basis of infrared spectrum and molecular-weight analogies with the other complexes. The difference in analytical figures for the two possible structures is not sufficiently large to differentiate, and it is unfortunate that a direct analysis for oxygen in presence of phosphorus is not possible. It may be noted, however, that the value of the conductivity [$\mu = 0{\cdot}66$ ohm^{-1} $cm.^2$, V(l./mole) = 541] quoted by Hieber and Schuster as evidence for the ionic structure $[(Ph_3P)_2Re(CO)_4]^+Cl^-$, appears to be rather low for an ionic compound;

[6] Hieber and Fuchs, *Z. anorg. Chem.*, 1941, **248**, 269.
[7] Hieber and Schuster, *ibid.*, 1956, **287**, 214.

for acetone solutions, Reynolds and Kraus [8] give values of $\mu = 100$ ohm^{-1} cm.^{2} for ionic compounds, and for a very bulky ionic species, hexaformylpiperidineiron tridecacarbonyl tetraferrate, a value $\mu = 249$ ohm^{-1} cm.^{2} has recently been reported.[9] We have in fact found conductivities of the same order as for the triphenylphosphine complex for the rhenium pentacarbonyl halides themselves, *viz.*, $Re(CO)_5Cl$ [$\mu = 0{\cdot}48$ ohm^{-1} cm.^{2}, V(l./mole) = 200], $Re(CO)_5Br$ [$\mu = 0{\cdot}22$ ohm^{-1} cm.^{2}, V(l./mole) = 156], $Re(CO)_5I$ [$\mu = 0{\cdot}16$ ohm^{-1} cm.^{2}, V(l./mole) = 132]. These small values can reasonably be regarded as due to the

TABLE 2. *Substituted carbonyl halides of manganese and rhenium.*

Compound	Colour	Method of preptn.	CO stretching modes (cm.$^{-1}$)
$Mn(CO)_3I(Py)_2$	Dark yellow	A + B	2037, 1954, 1906
$Mn(CO)_3IDipy$	Dark orange	A	2036, 1943, 1929
$Mn(CO)_3Cl(Ph_3P)_2$	Cream	B	2049, 1954, 1917
$Mn(CO)_3Br(Ph_3P)_2$	Light brown	A	2046, 1955, 1916
$Mn(CO)_3I(Ph_3P)_2$	Light brown	A	2042, 1955, 1915
$Mn(CO)_3Cl(Ph_3As)_2$	Yellow	B	2050, 1960, 1915
$Mn(CO)_3Br(Ph_3As)_2$ ...	Orange	A	2025, 2055, 1958 (w), 1918 (w)
$Mn(CO)_3I(Ph_3As)_2$	Dark orange	A + B	2012, 2041, 1955 (w), 1918 (w)
$Re(CO)_3Cl(Py)_2$	White	A	2041, 1934, 1891
$Re(CO)_3I(Py)_2$	Cream	B	2041, 1934, 1891
$Re(CO)_3IDipy$	Yellow	A	2037, 1932, 1903
$Re(CO)_3Cl(Ph_3P)_2$	White	A	2050, 1961, 1901
$Re(CO)_3I(Ph_3P)_2$	Cream	A	2049, 1966, 1904
$Re(CO)_3Cl(Ph_3As)_2$	White	B	2049, 1960, 1904
$Re(CO)_3I(Ph_3As)_2$	Pale yellow	A + B	2047, 1961, 1908

slight ionic character of the Re–X bond in these compounds. Finally, the sample of $(Ph_3P)_2Re(CO)_3Cl$ obtained quantitatively from the reaction of the phosphine with rhenium *tetracarbonyl* chloride with evolution of carbon monoxide is identical with product from the pentacarbonyl chloride. The formulation of the phosphine complex as a tetracarbonyl complex thus appears to be eliminated.

Efforts to produce monosubstitution derivatives of the rhenium and manganese pentacarbonyl halides have not been successful, and all attempts to substitute more than two carbonyl groups have resulted in complete decomposition of the molecule. Substituted carbonyl halides in which the bridging structure is intact have not been obtained.

EXPERIMENTAL

Microanalyses and molecular-weight measurements are by the Microanalytical Laboratory of Imperial College.

Preparations and Techniques.—Infrared spectra were recorded in chloroform on a model 21 Perkin-Elmer double-beam spectrometer, with sodium chloride optics. Conductivity was measured in anhydrous acetone with a Type E.7566 Mullard bridge. Rhenium carbonyl halides and manganese pentacarbonyl iodide were prepared as previously described.[1,5]

Preparation of Manganese Pentacarbonyl Chloride.—A slow stream of chlorine was passed into manganese carbonyl (4·00 g.) in carbon tetrachloride (75 c.c.) at 0°. Pale yellow crystals were rapidly precipitated in the exothermic reaction, but were soon obscured by the precipitation of manganese chloride as a fine white powder. After 20 min. the flow of gas was stopped and volatile matter removed (20°/10 mm.). From the residual solid was sublimed (40°/0·1 mm.) pure *manganese pentacarbonyl chloride* (3·03 g., 64%) [Found: C, 26·2; Cl, 15·5; O, 34·8. $Mn(CO)_5Cl$ requires C, 26·0; Cl, 15·4; O, 34·7%].

Preparation of Manganese Pentacarbonyl Bromide.—Bromine (2·46 g., 1·3 mol.) was added to manganese carbonyl (4·6 g., 1 mol.) in carbon tetrachloride (50 c.c.), and the mixture gently shaken at 40°. Carbon monoxide was evolved and considerable manganese bromide was precipitated. After 1 hr. volatile matter was removed (20°/10 mm.). The residual solid mass was washed with water (3 × 25 c.c.) and after drying was sublimed (55°/0·1 mm.), to give

[8] Reynolds and Kraus, *J. Amer. Chem. Soc.*, 1948, **70**, 1709.
[9] Hieber and Kahlen, *Chem. Ber.*, 1958, **91**, 2223.

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manganese pentacarbonyl bromide (4·75 g., 73%) [Found: C, 21·6; Br, 29·1; O, 30·0. $Mn(CO)_5Br$ requires C, 21·8; Br, 29·1; O, 29·1%].

Thermal Decomposition of the Manganese Pentacarbonyl Halides. Reaction (1).—The pentacarbonyl halides (*ca.* 1·0 g.) in light petroleum (b. p. 100—120°) were heated under reflux in a stream of nitrogen. After 1 hr. heating was stopped and a mixture of dark crystals and fine powder separated. After removal of solvent (20°/0·1 mm.) and washing with water (3 × 25 c.c.), then drying, the residue was extracted with hot benzene (3 × 10 c.c.) and the filtered extract cooled (0°). Fine crystals of the tetracarbonyl halides separated, and after decantation of the liquid these were washed rapidly with light petroleum (5 c.c.) and then excess of solvent was removed (20°/0·1 mm.) to leave the pure product (Table 3).

TABLE 3.

Compound	Yield (%)	Mol. wt. Found	Mol. wt. Calc.	Found (%) C	Found (%) O	Found (%) Hal.	Required (%) C	Required (%) O	Required (%) Hal.
$[Mn(CO)_4Cl]_2$	45	425	403	24·1	30·8	17·1	23·8	31·6	17·6
$[Mn(CO)_4Br]_2$	53	476	494	19·6	25·5	32·2	19·5	26·1	32·4
$[Mn(CO)_4I]_2$	47	629	588	16·4	22·5	42·1	16·3	21·8	43·2

Interaction of Carbon Monoxide and the Manganese Tetracarbonyl Halides.—The finely powdered tetracarbonyl halide (*ca.* 0·5 g.) was placed under carbon monoxide in a metal autoclave at 180°/150 atm. After cooling, a fall in the initial pressure was observed. The contents of the cooled autoclave were extracted with benzene, and after filtration of the solution and removal of solvent (20°/10 mm.) the crude product was subimed to give the pure pentacarbonyl halide (Table 4).

TABLE 4.

Compound	Yield (%)	Found C	Found O	Calc. C	Calc. O	CO stretching modes ($cm.^{-1}$)
$Mn(CO)_5Cl$	74	25·8	34·8	26·0	34·7	2072, 2015
$Mn(CO)_5I$	82	18·0	24·0	18·3	24·8	2055, 2018

Interaction of Manganese and Rhenium Pentacarbonyl Halides with Certain Ligands. Method (*A*). *Reaction* (2).—The carbonyl halide (*ca.* 0·1 g.) was heated (120°) in nitrogen with an excess (*ca.* 5 mols.) of the ligand. Heating was continued (*ca.* 30 min.) until the steady stream of carbon monoxide ceased. After cooling, excess of ligand was removed by washing with ether (3 × 5 c.c.). The residual solid was extracted with chloroform in the cold (2 × 2 c.c.), and to the filtered chloroform solution was added light petroleum (15 c.c.). The solution was allowed to crystallise overnight, and after removal of mother liquor the crystals were washed with light petroleum (2 × 2 c.c.) and excess of solvent was removed (20°/0·1 mm.) to leave the pure product (Table 5).

TABLE 5 (*Method A*).

Compound	Yield (%)	Found (%) C	H	O	N	P	As	Hal.	Required (%) C	H	O	N	P	As	Hal.
$Me(CO)_3IPy_2$	74	36·8	2·8	11·4	6·9				36·8	2·4	11·3	6·6			
$Mn(CO)_3IDipy$	81	37·0	2·2	11·5	6·6			29·8	37·0	1·9	11·4	6·6			30·0
$Mn(CO)_3Br(Ph_3P)_2$...	67	63·5	4·4					10·2	63·1	4·0					10·8
$Mn(CO)_3I(Ph_3P)_2$ ...	81	58·3	4·0			7·3		15·9	59·2	3·8			7·8		16·1
$Mn(CO)_3Br(Ph_3As)_2$	72	57·0	4·2				18·4		56·3	3·6				18·1	
$Mn(CO)_3I(Ph_3As)_2$ ...	67	52·8	3·6	5·2			17·2		53·4	3·4	5·5			17·1	
$Re(CO)_3ClPy_2$	77	33·1	1·9		6·4				33·6	2·2		6·0			
$Re(CO)_3IDipy$	74	28·9	1·8	8·7	5·3			23·6	28·2	1·5	8·7	5·1			22·9
$Re(CO)_3Cl(Ph_3P)_2$ ...	65	56·4	4·2			7·4		4·5	56·5	3·6			7·5		4·3
$Re(CO)_3I(Ph_3P)_2$ ...	79	50·9	3·7			6·6			50·9	3·3			6·7		
$Re(CO)_3I(Ph_3As)_2$ ...	68	46·3	3·1	4·5			15·1		46·4	3·0	4·4			14·9	

Interaction of Manganese and Rhenium Tetracarbonyl Halides with Certain Ligands. Method (*B*). *Reaction* (3).—The procedure adopted was the same as that adopted for the pentacarbonyl halide reactions described above. It was noted, however, that the reaction in general started

at a temperature about 20° lower in each case and on this scale was completed at 120° in 15 min. (Table 6).

TABLE 6 (*Method B*).

Compound	Yield (%)	Found (%)					Required (%)				
		C	H	O	As	Hal.	C	H	O	As	Hal.
$Mn(CO)_3I(Py)_2$	67	36·6	2·9	11·7			36·8	2·4	11·3		
$Mn(CO)_3Cl(Ph_3P)_2$	74	62·8	4·7				62·0	4·3			
$Mn(CO)_3Cl(Ph_3As)_2$ ...	61	59·9	4·5			4·1	59·5	3·8			4·5
$Mn(CO)_3I(Ph_3As)_2$	56	53·2	3·8			14·9	53·2	3·4			14·5
$Re(CO)_3Cl(Ph_3As)_2$ ...	77	50·8	3·6		16·9		51·0	3·3		16·4	
$Re(CO)_3I(Ph_3As)_2$	61	46·2	3·5	4·9			46·4	3·0	4·4		

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292. *Spectrophotometric Evidence for the Solvation of Halogenopalladate(II) Ions by Various Polar Solvents.*

By C. M. HARRIS, S. E. LIVINGSTONE, and I. H. REECE.

The visible and ultraviolet spectra of the halogenopalladate(II) ions $[PdX_4]^{2-}$ (X = Cl or Br) and $[Pd_2X_6]^{2-}$ (X = Cl, Br, or I) have been measured in a range of polar solvents and in the solid state. The two ionic species $[PdX_4]^{2-}$ and $[Pd_2X_6]^{2-}$ exhibit absorption maxima at the same wavelengths in the same solvent. Solutions of the bromo-complexes display a progressive shift of the maxima towards shorter wavelengths if the solvents are arranged in the sequence: $Ph{\cdot}NO_2$, Ac_2O, $Me{\cdot}NO_2$, $COMe_2$, MeOH, MeCN, H_2O. This is attributed to the formation of sexicovalent solvated ions, particularly since the maxima occur at much longer wavelengths in the spectra of the solid compounds. Similar results were obtained for the chloro- and iodo-palladate(II) complexes.

BIVALENT palladium usually forms quadricovalent complexes which are diamagnetic and square-planar. This configuration is associated with $4d5s5p^2$ hybridisation of the palladium atomic orbitals. This square-planar arrangement has been verified by *X*-ray structure determinations on a number of complexes.[1] Recently, complexes of bivalent palladium with a co-ordination number greater than four have been described. The ligand *o*-phenylenebisdimethylarsine (diarsine) forms sexicovalent complexes of the type $[Pd(diarsine)_2X_2]$ (X = Cl, Br, I, NO_2, or SCN).[2] The di-iodo-complex possesses a distorted *trans*-octahedral structure in the solid state.[3] In nitrobenzene solution these complexes behave as apparently quinquecovalent uni-univalent electrolytes, $[Pd(diarsine)_2X]X$. The sixth co-ordination position is most likely occupied by a molecule of solvent. Dimethyl-*o*-methylthiophenylarsine (thioarsine) forms compounds of the general formula, $Pd(thioarsine)_2X_2$ (X = Cl, Br, or I), which also probably possess a distorted octahedral structure in the solid state.[4] The higher complexes $[PdCl_5]^{3-}$ and $[PdCl_6]^{4-}$ have been postulated to occur in aqueous solution containing the $[PdCl_4]^{2-}$ ion and excess of chloride ion.[5] Harris, Livingstone, and Reece,[6] by a continuous-variation

[1] Wells, "Structural Inorganic Chemistry," Oxford University Press, 1950, p. 645.
[2] Harris and Nyholm, *J.*, 1956, 4375.
[3] Harris, Nyholm, and Stephenson, *Nature*, 1956, **177**, 1127.
[4] Livingstone, *Chem. and Ind.*, 1957, 143; *J.*, 1958, 4222.
[5] Sundaram and Sandell, *J. Amer. Chem. Soc.*, 1955, **77**, 855.
[6] Harris, Livingstone, and Reece, *Austral. J. Chem.*, 1957, **10**, 282.

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spectrophotometric study, have demonstrated the formation of the $[PdBr_6]^{4-}$ ion in nitrobenzene solutions of tetraethylammonium tetrabromopalladate(II) upon the addition of bromide ions. The existence of sexicovalent palladium complexes such as $[Pd(diarsine)_2X_2]$ has been attributed to the use by the palladium atom of two additional $5p5d$ bonds normal to the plane of the four $4d5s5p^2$ hybrid bonds.[2,3] Sexicovalent structures of this type would be expected to possess a distorted octahedral arrangement due to the repulsion of the filled non-bonding $4d_z^2$ orbital towards the bonding orbitals of the donor atoms of the ligand in the *trans*-octahedral positions.

The $[PdBr_4]^{2-}$ ion in nitrobenzene solution displays a strong absorption maximum at 427 mμ; the extinction coefficient at this wavelength is appreciably lowered by the addition of excess of bromide ion.[6] We have investigated further this reaction in methanol and water, so that the spectra could be obtained at shorter wavelengths and high concentrations of bromide ion. In Fig. 1 is shown the absorption spectrum in the visible and the ultraviolet region of the $[PdBr_4]^{2-}$ ion in M-perchloricacid; this acid was used to prevent hydrolysis of the $[PdBr_4]^{2-}$ ion, since the perchlorate ion does not form complexes with

FIG. 1. *Absorption spectra of* $K_2[PdBr_4]$: (I) *in* 1M-$HClO_4$; (II) *in water containing* Br^- *ions in* 20,000*-fold excess* (*see Experimental section*).

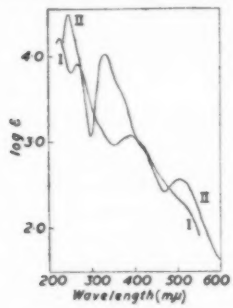
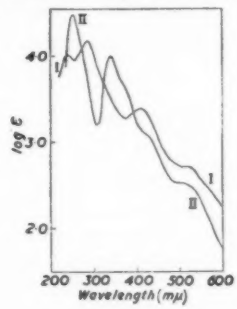


FIG. 2. *Absorption spectra of* $[NEt_4]_2[PdBr_4]$: (I) *in* MeOH; (II) *in* MeOH *containing* NEt_4Br *in* 1000*-fold excess* (*see Experimental section*).



palladium.[7] This spectrum differs markedly from that of an aqueous solution of $[PdBr_4]^{2-}$ ions containing a large excess of bromide ions. Similar results are recorded in Fig. 2 for the $[PdBr_4]^{2-}$ ion in methanol with and without bromide ions. Whilst the spectra of solutions of $[PdBr_4]^{2-}$ ion in the presence of a large excess of bromide ion in methanol and water are very similar (see Table 1), owing to the formation of one or more higher complexes of bivalent palladium, it can be seen that there is a marked difference between the spectra

TABLE 1. *Wavelengths* (λ *in* mμ) *and extinction coefficients* (ε) *of maxima in the absorption spectra of tetrabromopalladate*(II) *ion in water and methanol solutions containing excess of bromide ion.**

Solvent	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε
Water	505	370	332	10,400	247	31,400
Methanol	508	335	341	10,000	252	31,600

* See Experimental section for concentrations used.

of the $[PdBr_4]^{2-}$ ion in methanol and aqueous M-perchloric acid, in that the absorption maxima are shifted to shorter wavelengths in water (see Table 2). This suggested strongly that the donor properties of the solvent affect the wavelengths of the maximum absorptions, owing to the formation of solvated $[PdBr_4]^{2-}$ ions, and led us to measure the spectra of the $[PdBr_4]^{2-}$ ion in a variety of solvents. The spectra of the dimeric halogen-bridged species $[Pd_2Br_6]^{2-}$ were also investigated for comparison, as we have recently

[7] Livingstone, *J.*, 1957, 5091.

shown that this ion exists in acetone and nitrobenzene solutions as well as in the solid state.[8] The wavelengths and extinction coefficients of the absorption maxima are listed in Table 2.

TABLE 2. *Wavelengths* (λ *in* mμ) *and extinction coefficients* (ε) *of maxima in the absorption spectra of tetrabromopalladate*(II) *and tetrabromo-*$\mu\mu'$*-dibromodipalladate*(II) *ions in various solvents.*

Solvent	Compound	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε
$Ph{\cdot}NO_2$	$[NEt_4]_2[PdBr_4]$	524	490	427	2600	*a*	—	*a*	—
"	$[NEt_4]_2[Pd_2Br_6]$	525 (sh)	850	427	4750	*a*	—	*a*	—
Ac_2O	$[NEt_4]_2[PdBr_4]$	522	450	425	2800	*a*	—	*a*	—
"	$[NEt_4]_2[Pd_2Br_6]$	520	900	424	5600	*a*	—	*a*	—
$Me{\cdot}NO_2$	$[NEt_4]_2[PdBr_4]$	510	400	419	2600	*a*	—	*a*	—
"	$[NEt_4]_2[Pd_2Br_6]$	513	800	419	5300	*a*	—	*a*	—
$COMe_2$	$[NEt_4]_2[PdBr_4]$	*b*	—	412	1320	*a*	—	*a*	—
"	$[NEt_4]_2[Pd_2Br_6]$	*b*	—	412	2750	*a*	—	*a*	—
MeOH	$[NEt_4]_2[PdBr_4]$	510	520	411	2400	285	15,000	241	10,500
"	$[NEt_4]_2[Pd_2Br_6]$	512 (sh)	600	411	4300	280	22,000	242	20,000
MeCN	$[NEt_4]_2[PdBr_4]$	*b*	—	410	1700	274 [c]	23,000	—	—
"	$[NEt_4]_2[Pd_2Br_6]$	*b*	—	411	4000	273 [d]	52,000	—	—
H_2O (1M-$HClO_4$)	$K_2[PdBr_4]$	500	220	391	1200	268	8000	227	16,000

[a] Solvent absorbs in this region. [b] A broad shoulder in the region 520—480 mμ. [c] Also a maximum at 327 mμ (ε 2300). [d] Also a maximum at 327 mμ (ε 5300). sh = shoulder.

In general, these two ionic species $[PdBr_4]^{2-}$ and $[Pd_2Br_6]^{2-}$ exhibit maxima at the same wavelengths in the same solvent. The extinction coefficients of the maxima of the dimeric ion are in most instances approximately double those of the monomeric species. The maxima shift towards shorter wavelengths if the solvents are arranged in the order: $Ph{\cdot}NO_2$, Ac_2O, $Me{\cdot}NO_2$, $COMe_2$, MeOH, MeCN, H_2O. It is not unreasonable to assume that this series indicates the order of increasing strength of attachment of solvent molecules to the palladium atom. Water appears in this series as the solvent with the strongest donor property. The compound $[Pd(H_2O)_4](ClO_4)_2$ is not dehydrated *in vacuo* over phosphoric oxide;[7] this indicates that the water molecules are firmly attached. The general shift of the absorption maxima of the bromopalladate(II) ions is most marked in the case of the second absorption band in the range 427—391 mμ; the other two bands in the ultraviolet region appear to follow a similar trend in those solvents in which measurements could be made. The same general shift to shorter wavelengths was also observed for the chloropalladate(II) species $[PdCl_4]^{2-}$ and $[Pd_2Cl_6]^{2-}$ (see Table 3). Again

TABLE 3. *Absorption maxima* (mμ) *and extinction coefficients* (ε) *of tetrachloropalladate*(II) *and tetrachloro-*$\mu\mu'$*-dichlorodipalladate*(II) *ions in various solvents.*

Solvent	Compound	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε
$Ph{\cdot}NO_2$	$[AsPh_3Me]_2[Pd_2Cl_6]$	441	650	*a*	—
Ac_2O	$[AsPh_3Me]_2[Pd_2Cl_6]$	439	620	345	4000
$MeNO_2$	$[AsPh_3Me]_2[PdCl_4]$	437	190	*a*	—
"	$[AsPh_3Me]_2[Pd_2Cl_6]$	439	460	*a*	—
$COMe_2$	$[AsPh_3Me]_2[Pd_2Cl_6]$	440	600	340 (br)	2800
MeOH	$[AsPh_3Me]_2[Pd_2Cl_6]$	431	750	320	2600
MeCN	$[AsPh_3Me]_2[PdCl_4]$	452 (sh), 400	200, 250	332	1200
"	$[AsPh_3Me]_2[Pd_2Cl_6]$	455 (sh), 400	350, 490	332	2300
H_2O (M-$HClO_4$)	$K_2[PdCl_4]$	426	220	305 (sh)	730

[a] Solvent absorption in this region. sh = shoulder; br = broad.

the most pronounced shift occurs in the second absorption band (345—305 mμ). In Table 4 are listed the absorption maxima for the $[Pd_2I_6]^{2-}$ ion; in the limited number of solvents in which this species is soluble, the same general tendency is observed. The ion $[Pd_2I_6]^{2-}$ also displays a broad absorption in the region 750—700 mμ (*e.g.*, see spectrum in

[8] Harris, Livingstone, and Stephenson, *J.*, 1958, 3697.

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acetone, Fig. 3); no definite maximum could be determined. It seems that in this region is located the first absorption band, which corresponds to the bands at 525—500 mμ and 441—426 mμ for the bromo- and chloro-species, respectively.

TABLE 4. *Absorption maxima* (mμ) *and extinction coefficients* (ε) *of the tetraiodo-μμ'-di-iodo-dipalladate*(II) *ion in various solvents.*

Solvent	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε
$Ph{\cdot}NO_2$	536	8100	452	11,200	*a*	—
$Me{\cdot}NO_2$	524	7200	448	9900	*a*	—
$COMe_2$	531	6700	447	9200	342	36,000
MeCN	528	7200	447	9500	339	40,000

[a] Solvent absorbs in this region.

Sundaram and Sandell [5] have postulated the formation of the ions $[PdCl_5]^{3-}$ and $[PdCl_6]^{4-}$ in aqueous perchloric acid solutions of $[PdCl_4]^{2-}$ from shifts of the absorption maximum in the visible region upon the addition of chloride ions. In Fig. 4 are shown the absorption spectra of solutions of potassium chloropalladate(II) in both M-perchloric acid and 10M-hydrochloric acid. It can be seen that the spectrum of the hydrochloric acid solution is also markedly altered in the ultraviolet region.

FIG. 3. *Absorption spectrum of* $[NEt_4]_2[Pd_2I_6]$ *in acetone.*

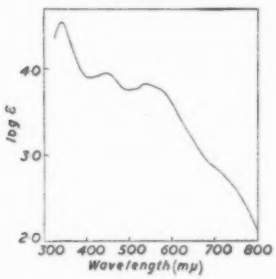


FIG. 4. *Absorption spectra of* K_2PdCl_4: (I) *in* 1M-$HClO_4$ [$\lambda_{max.}$ 426, ε 220; $\lambda_{max.}$ 305 (sh), ε 730]; (II) *in* 10M-HCl [$\lambda_{max.}$ 472, ε 170; $\lambda_{max.}$ 330 (sh), ε 650; $\lambda_{max.}$ 278, ε 12,000].

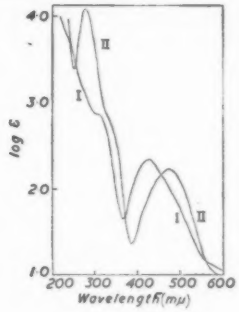
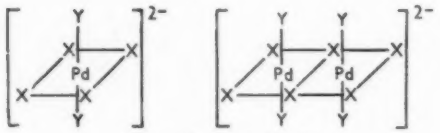


FIG. 5.



(Y = solvent molecule)

As mentioned above, bivalent palladium in certain instances exhibits a distorted octahedral configuration, and our results suggest that both species $[PdX_4]^{2-}$ (X = Cl or Br) and $[Pd_2X_6]^{2-}$ (X = Cl, Br, or I) in solution form solvated ions, which are no doubt further examples of a distorted octahedral arrangement of bivalent palladium (Fig. 5).

The compound $K_2[PdCl_4]$ has been shown to be isomorphous with the square-planar complex $K_2[PtCl_4]$ [9]: *X*-ray crystal analysis of the compound $[NEt_4]_2[Pt_2Br_6]$ has confirmed the existence of the discrete planar bromo-bridged anion $[Pt_2Br_6]^{2-}$. A powder photograph of the analogous palladium compound $[NEt_4]_2[Pd_2Br_6]$ is similar to that of

[9] Dickinson, *J. Amer. Chem. Soc.*, 1922, **44**, 2404.

the platinum compound, indicating a planar configuration about the palladium atoms.[8] Consequently, we examined the absorption spectra of the halogenopalladate(II) complexes in the solid state (see Figs. 6—12). The absorption maxima are listed in Table 5.

TABLE 5. *Absorption maxima* (mμ) *of halogenopalladate*(II) *complexes in the solid state.*

$K_2[PdCl_4]$	600 (sh)	465 (s)	310 (sh), 275 (s)	$K_2[PdBr_4]$	625 (sh)	500 (s)	—	385 (s)
$[AsPh_3Me]_2[PdCl_4]$	—	485 (s), 430 (w, sh)	300 (s)	$[NEt_4]_2[PdBr_4]$	—	520 (s)	450 (sh)	400 (s), 360 (s)
$[AsPh_3Me]_2[Pd_2Cl_6]$	—	500 (sh), 450 (s)	325 (s)	$[NEt_4]_2[Pd_2Br_6]$	—	525 (s)	440 (s)	325 (s)
				$[NEt_4]_2[Pd_2I_6]$	700 (sh)	585 (s)	475 (s)	370 (s, br)

(s = strong; sh = shoulder; w = weak; br = broad.)

The first peak was not observed in the spectra of the chloro- and bromo-complexes containing the cations $[AsPh_3Me]^+$ and $[NEt_4]^+$, respectively. It seems reasonable to

FIG. 6. FIG. 7. FIG. 8.

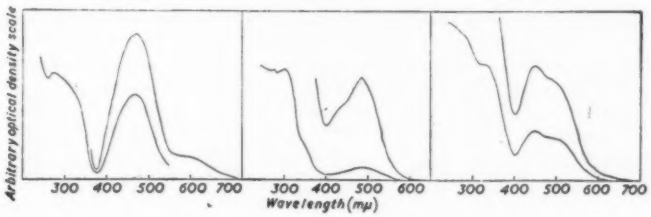


FIG. 9. FIG. 10. FIG. 11.

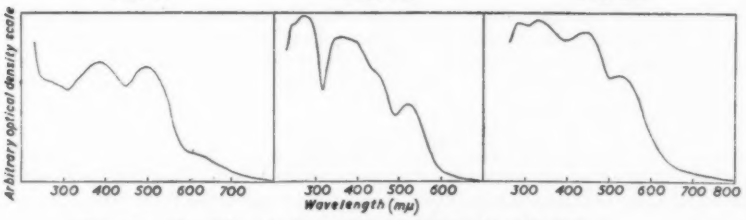
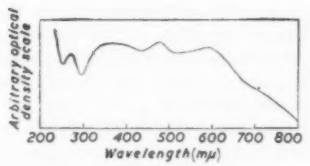


FIG. 6. *Absorption spectrum of* $K_2[PdCl_4]$ *in the solid state.*
FIG. 7. *Absorption spectrum of* $[AsPh_3Me]_2[PdCl_4]$ *in the solid state.*
FIG. 8. *Absorption spectrum of* $[AsPh_3Me]_2[Pd_2Cl_6]$ *in the solid state.*
FIG. 9. *Absorption spectrum of* $K_2[PdBr_4]$ *in the solid state.*
FIG. 10. *Absorption spectrum of* $[NEt_4]_2[PdBr_4]$ *in the solid state.*
FIG. 11. *Absorption spectrum of* $[NEt_4]_2[Pd_2Br_6]$ *in the solid state.*

FIG. 12. *Absorption spectrum of* $[NEt_4]_2[Pd_2I_6]$ *in the solid state.*



correlate the bands obtained for solid $K_2[PdCl_4]$ at 600 and 465 mμ with those bands obtained for solutions of the chloropalladate(II) complexes at 441—426 and 345—305 mμ, respectively. Similarly, the three bands of solid $K_2[PdBr_4]$ at 625, 500, and 385 mμ can be correlated with the solution bands at 524—500, 427—391, and 285—268 mμ, respectively. The bands for the solid iodo-complex at 585, 475, and 370 mμ can be compared with the solution bands at 536—528, 452—447, and 342—339 mμ, respectively, while the

shoulder at 700 mμ would correspond to the broad absorption occurring at about this wavelength in the solutions. The occurrence of the maxima at much higher wavelengths in the spectra of the solid complexes, which contain quadricovalent palladium, than in to the spectra of the complexes in solution, is in keeping with the postulate of sexicovalent solvated palladium complex ions in polar solvents. A comparison of the spectra of the solid compounds with those of the solution shows that the magnitude of the shift of the maxima to shorter wavelengths is in the order, chloro- > bromo- > iodo-, for these complexes.

Chatt *et al.*,[10] from a study of the visible and ultraviolet spectra of platinum(II) ammines, have concluded that bivalent platinum in these compounds shows little, if any, tendency to form sexicovalent complexes. It is noteworthy that the absorption spectra of the $[PtCl_4]^{2-}$ ion, unlike those of the $[PdCl_4]^{2-}$ ion, are virtually identical in 1M-perchloric acid and 10M-hydrochloric acid, and that the absorption maxima are not markedly different from those obtained in the solid state (see Table 6).

TABLE 6. *Absorption maxima* (mμ) *and extinction coefficients* (ε) *of potassium tetrachloroplatinate*(II).

Solvent	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε
1M-$HClO_4$	471	16·5	388	51	321	80
1M-HCl	477	15·8	390	59	330	62
2M-HCl (ref. 10)	476	15	392	59	331	64
10M-HCl	475	16·5	388	63	324	76
(Solid) (refs. 10, 11)	500	—	375	—	340	—

Although bivalent platinum in these complexes shows little tendency to increase its covalency beyond four, the compounds $[Pt(diarsine)_2I_2]$ [3] and $Pt^{IV}(NH_3)_2Br_4$, $Pt^{II}(NH_3)_2Br_2$ [12] contain a distorted octahedral configuration about the bivalent platinum atom in the solid state. In the triad Ni, Pd, Pt it would appear that the tendency to form sexicovalent complexes decreases in the order $Ni^{II} > Pd^{II} > Pt^{II}$.

EXPERIMENTAL

Preparation of Compounds.—Potassium tetrachloropalladate(II). Palladium sponge was dissolved in aqua regia and the solution taken to dryness twice with hydrochloric acid. The residue was dissolved in hot 0·5M-hydrochloric acid, and the calculated quantity of potassium chloride added. The hot solution was filtered to remove traces of potassium hexachloropalladate(IV), and on cooling, deposited crystals of the compound, which was recrystallised from 0·5M-hydrochloric acid (Found: Pd 32·6. Calc. for Cl_4K_2Pd: Pd, 32·6%).

Potassium tetrabromopalladate(II). Palladium sponge was dissolved in 48% hydrobromic acid containing a little concentrated nitric acid. The solution was taken almost to dryness several times with hydrobromic acid, the residue dissolved in hot 0·5M-hydrobromic acid, and the calculated quantity of potassium bromide added. Concentration and cooling of the solution gave dark red crystals which were recrystallised from 0·5M-hydrobromic acid, washed with 0·5M-hydrobromic acid, then acetone, and dried at 150° (Found: Br, 63·3. Calc. for Br_4K_2Pd: Br, 63·4%).

Potassium tetrachloroplatinate(II). This compound, prepared as described by Gil'dengershel and Shagisultanova,[13] was recrystallised from 0·5M-hydrochloric acid and dried (Found: Pt, 46·9. Calc. for Cl_4K_2Pt: Pt, 47·0%).

The following compounds were prepared as described in the references:

Tetraethylammonium tetrabromopalladate(II) [6] (Found: C, 27·8; H, 6·2; N, 3·9; Br, 46·5; Pd, 15·5. Calc. for $C_{16}H_{40}N_2Br_4Pd$: C, 28·0; H, 5·9; N, 4·1; Br, 46·5; Pd, 15·5%).

[10] Chatt, Gamlen, and Orgel, *J.*, 1958, 486.
[11] Yamada, *J. Amer. Chem. Soc.*, 1951, **73**, 1182.
[12] Brosset, *Arkiv Kemi, Min., Geol.*, 1948, **25**, No. 19.
[13] Gil'dengershel and Shagisultanova, *Zhur. priklad. Khim.*, 1953, **27**, 222.

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Tetraethylammonium tetrabromo-μμ′-dibromodipalladate(II) [6] (Found: C, 20·4; H, 4·4; N, 2·8; Br, 49·7; Pd, 22·4. Calc. for $C_{16}H_{40}N_2Br_6Pd_2$: C, 20·2; H, 4·2; N, 2·9; Br, 50·2; Pd, 22·4%).

Triphenylmethylarsonium tetrachloropalladate(II) [8] (Found: Cl, 15·9; Pd, 12·0. Calc. for $C_{38}H_{36}Cl_4As_2Pd$: Cl, 15·9; Pd, 12·0%).

Triphenylmethylarsonium tetrachloro-μμ′-dichlorodipalladate(II) [8] (Found: Cl, 19·9; Pd, 20·0. Calc. for $C_{38}H_{36}Cl_6As_2Pd_2$: Cl, 19·9; Pd 20·0%).

Tetraethylammonium tetraiodo-μμ′-di-iododipalladate(II) [8] (Found: C, 15·6; H, 3·4; N, 2·2; Pd, 17·3. Calc. for $C_{16}H_{40}N_2I_6Pd_2$: C, 15·6; H, 3·3; N, 2·3; Pd, 17·3%).

Solvents.—The acetone and methanol were of " AnalaR " quality and were dry. Nitromethane was distilled, dried ($CaCl_2$), and then twice fractionated (b. p. 100·5°). Nitrobenzene was washed with water, dried ($CaCl_2$), and distilled; the distillate was purified by freezing, followed by fractional distillation at 10 mm. from P_2O_5. " AnalaR " acetic anhydride was further purified by fractional distillation. Acetonitrile (Hopkin and Williams) was distilled from P_2O_5 (b. p. 81·4—81·8°), then again fractionally distilled (b. p., 81·6—81·7°).

The compounds $[NEt_4]_2[PdBr_4]$ and $[NEt_4]_2[Pd_2Br_6]$ recrystallised unchanged from acetonitrile, indicating that acetonitrile does not replace the bromo-groups.

Measurement of Spectra.—Spectra were recorded on a Cary 11-MS-50 Spectrophotometer. The solids were examined as Nujol mulls in the manner of infrared samples. This necessitated fine grinding to minimise the scattering of radiation and for the potassium salts, in which this effect was most pronounced, a vibration ball mill was used. Samples containing organic residues were easily prepared. The instrument was balanced against two matched scatter-plates of rock-salt, roughened on both sides with emery paper. The mull was then spread on one side of the scatter-plate that had been in the " sample " compartment for balancing and, when required for thinning out the film, a clear rock-salt plate was pressed on to it. In this fashion the amount of scattering produced by the sample was generally only a little more than that which would be produced by one side of the doubly roughened scatter-plate. Roughening the second side of the sample-plate made the process of recording spectra much simpler since this prevented light from passing through clearer spaces in the mull and falling directly on the detector. Thus the position equivalent to 100% absorption was displaced to a reading of higher optical density, since the instrument recorded in optical density rather than in per cent. transmission. The spectra are essentially " as recorded " and are meant to indicate little more than the location of absorption bands. Correction has been made for scattering where this was more than for the reference plate; but where this effect was even as high as 85% more (optical density 0·8), the result was to raise the zero of absorption by the same amount at all wavelengths.

Spectra of Higher Bromo-complexes; see Figs. 1 *and* 2.—The spectra in water were measured on (*a*) a solution of $K_2[PdBr_4]$ (5×10^{-4}M) in constant-boiling hydrobromic acid (8·6M) for the range 600—375 mμ, and (*b*) a solution of $K_2[PdBr_4]$ (5×10^{-5}M) in M-potassium bromide for the range 400—235 mμ. In the range 400—375 mμ the extinction coefficients of both solutions were almost identical. Hydrobromic acid could not be used below 350 mμ owing to absorption by traces of bromine.

The spectra in methanol were obtained from (i) a solution of $[NEt_4]_2[PdBr_4]$ (10^{-3}M) in methanol containing tetraethylammonium bromide (1M) in the range 600—400 mμ. For the wavelength range 400—235 mμ, a solution of $[NEt_4]_2[PdBr_4]$ (10^{-4}M) in methanol, containing tetraethylammonium bromide (0·1M), was used. The value of ε at 400 mμ was the same for both solutions.

Microanalyses.—Microanalyses for carbon, hydrogen, and nitrogen were carried out by Dr. E. Challen, of the Microanalytical Laboratory of this University.

School of Applied Chemistry, University of New South Wales,
Broadway, Sydney, Australia. [*Received, October* 31*st*, 1958.]

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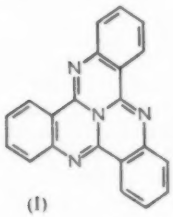
293. *Cyclic Amidines. Part VIII.* Derivatives of* 12H-6 : 7 : 12a-*Triazabenz*[a]*anthracene and* 5a*H*-5 : 6 : 11a-*Triazanaphthacene.*

By K. Butler and M. W. Partridge.

The formation of derivatives of the triazabenz[*a*]anthracene (II) and the triazanaphthacene (III) and their behaviour on alkylation are described. Interconversions of these ring systems were effected with certain derivatives.

The unusual carcinogenic properties of tri*cyclo*quinazoline [1] (I) prompted an investigation of triazatetracyclic compounds, for which there are six possible structures resulting from the fusion of two quinazoline rings and having one nitrogen atom common to the two rings. The work now reported relates to derivatives of 12*H*-6 : 7 : 12a-triazabenz[*a*]anthracene (II) and 5a*H*-5 : 6 : 11a-triazanaphthacene (III).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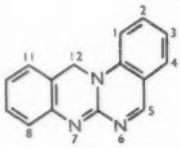
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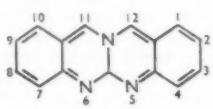
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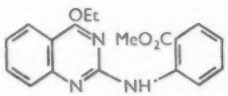
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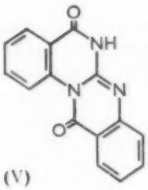
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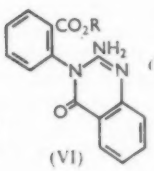
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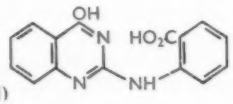
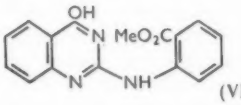
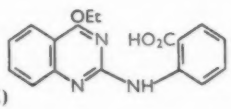
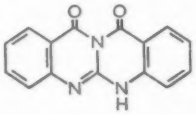

(VII)


(VIII)


(IX)


(X)

2-Chloro-4-ethoxyquinazoline and methyl anthranilate in ethanol yielded 4-ethoxy-2-*o*-methoxycarbonylanilinoquinazoline (IV). This compound, on being boiled with aqueous hydrochloric acid or with potassium hydroxide, afforded, according to the conditions, 5 : 6-dihydro-5 : 12-dioxo-12*H*-6 : 7 : 12a-triazabenz[*a*]anthracene (V) and/or 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazoline (VI; R = H) and not, as might have been expected, 2-*o*-carboxyanilino-4-hydroxyquinazoline (VII). With ethanolic potassium hydroxide, the products were 4-hydroxy-2-*o*-methoxycarbonylanilinoquinazoline (VIII), also synthesised directly from 2-chloro-4-hydroxyquinazoline and methyl anthranilate, and 2-*o*-carboxyanilino-4-ethoxyquinazoline (IX), otherwise obtained unequivocally by the treatment of anthranilic acid with 2-chloro-4-ethoxyquinazoline.

The structure assigned to the triazabenzanthracene (V) followed from its formation, in high yield, by direct cyclisation of 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazoline (VI; R = H).

Evidence for the constitution of 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazoline (VI; R = H) was provided by a comparison of its methyl ester (VI; R = Me) with the unequivocally synthesised isomer (VIII); they were different (Table 1). The ester (VIII) on being heated furnished the two possible cyclisation products, namely the

* Part VII, *J.*, 1958, 2086.

[1] Baldwin, Butler, Cooper, Partridge, and Cunningham, *Nature*, 1958, **181**, 838.

triazabenzanthracene (V), and its isomer, 11 : 12-dihydro-11 : 12-dioxo-5*H*-5 : 6 : 11a-triazanaphthacene (X), whereas the ester (VI; R = Me) gave, as expected, only the triazabenzanthracene (V). Furthermore, 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazoline (VI; R = H) formed a well-defined hydrochloride, whereas the hydrochloride of the isomer (VII), obtained from 2-chloro-4-hydroxyquinazoline and anthranilic acid, was unstable, and when heated in water cyclised to the triazabenzanthracene (V).

TABLE 1. *Ultraviolet absorption spectra in ethanol.*

Compound	Maxima (λ, mμ) and ε (in parentheses)					
(VI; R = Me)	218 (90,000)	290 (18,800)	330 (16,700)		382 (14,800)	
(VIII)	281 (17,500)	288 (18,000)	326 (14,100)			
(V)	235 (43,000)	283 (20,800)		320 (4,100)		335 (4,400)
(XV; R = Me)	236 (46,000)	283 (20,300)		325 (5,600)		
(XV; R = Et)	236 (51,000)	285 (21,800)		320 (5,960)		[335] 4,400
(XV; R = Pr[a])	236 (60,200)	284 (25,000)		320 (6,200)		
(XV; R = Bu[a])	235 (35,000)	285 (19,800)		320 (9,740)		
(XV; R = *n*-C_5H_{11})	234 (54,000)	282 (23,000)		320 (5,700)		
(XV; R = *n*-C_6H_{13})	235 (50,000)	282 (21,800)		320 (5,500)		
(XV; R = CH_2Ph)	236 (57,000)	282 (24,900)		320 (5,700)		
(XIV; R = Me)	235 (41,000)	283 (18,000)		320 (4,660)	[335] (4,350)	
(XIV; R = Et)	236 (55,000)	282 (24,000)		320 (5,300)	335 (4,800)	
(XVI; R = R′ = Me)	232 (24,300)	250 (16,600)	262 (14,400)	282 (21,600)	290 (28,000)	342 (15,500)
(XVI; R = R′ = Et)	[232] (24,000)	251 (15,800)	[263] (14,200)	282 (20,800)	291 (26,600)	342 (15,100)
(XVI; R = Me, R′ = Et)	[232] (24,000)	[251] (15,600)	[262] (14,000)	282 (21,800)	291 (26,600)	342 (15,900)

Data in [square] brackets refer to points of inflexion.

The ready cyclisation of this acid (VII) accounted for its absence from the products of treatment of 4-ethoxy-2-*o*-methoxycarbonylanilinoquinazoline (IV) with acids and alkalis. This property also implied that conversion of the ester (IV) into the triazabenzanthracene (V) in boiling aqueous acid involved the intermediate formation of a salt of the hydroxy-acid (VII). A similar cyclisation of the hydroxy-ester (VIII) to the triazabenzanthracene (V) was readily effected under the same conditions.

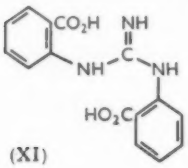
Formation of 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazoline (VI; R = H) from 4-ethoxy-2-*o*-methoxycarbonylanilinoquinazoline (IV) is probably an indirect process which included, in addition to the steps described above, a two-step degradation of the triazabenzanthracene (V) *via* the guanidine derivative (XI). The necessary fission of both heterocyclic rings was demonstrated by production of *NN*′-diphenylguanidine (XII) when a solution of the triazabenzanthracene (V) in two equivalents of sodium hydroxide was evaporated to dryness and heated with copper bronze in quinoline. The direct formation of the aminoquinazoline (VI; R = H) by fission of one ring of the triazabenzanthracene (V) is unlikely, since with only one equivalent of alkali, half of the tetracyclic compound remained undissolved; addition of hydrochloric acid to the alkaline filtrate afforded the hydrochloride of the aminoquinazoline (VI; R = H), formed, it is suggested, by cyclisation of the guanidine derivative (XI).

Heating of 2-chloro-4-ethoxyquinazoline and methyl anthranilate in the absence of solvent at 112° yielded ethyl chloride and a mixture of the triazabenzanthracene (V) and 4-hydroxy-2-*o*-methoxycarbonylanilinoquinazoline (VIII); before the onset of the exothermic phase of this reaction, the hydrochloride of the ester (IV) was isolable. This hydrochloride at 130° gave the same two products. Conversion of 4-hydroxy-2-*o*-methoxycarbonylanilinoquinazoline (VIII) into the mixture of the tetracyclic compounds (V) and (X), previously mentioned, occurred at 250°.

The triazabenzanthracene (V) and the triazanaphthacene (X) were interconverted when a solution of either in concentrated sulphuric acid was poured into methanol. In addition,

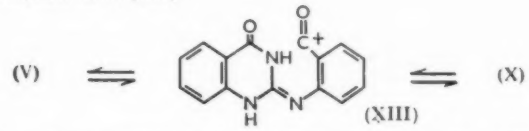
the methyl ester (VIII) was formed from both compounds. Accordingly, it is suggested that in sulphuric acid the cation (XIII) is in equilibrium with the cyclic compounds (V) and (X) or their cations.

The formation of the methyl ester (VIII) by reaction of the acylium ion (XIII) with methanol is then accounted for. Partial isomerisation to the linear system (X) was effected when a solution of the triazabenzanthracene (V) in concentrated sulphuric acid was poured into water. The linear compound (X) was slowly but almost quantitatively converted into the angular compound (V) when boiled in 2-ethoxyethanol.



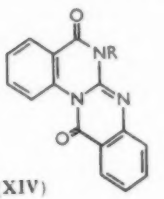
(XI)

NHPh·C(:NH)·NHPh (XII)

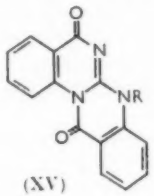


(V) (XIII) (X)

Methylation of the triazabenzanthracene (V) with methyl sulphate and sodium hydroxide afforded a 6- or 7-methyl derivative (XIV or XV; R = Me) which was stable to 48% hydrobromic acid and had an ultraviolet absorption spectrum very similar to the non-methylated compound (see Table 1). The same *N*-methyl derivative was formed when 2-*o*-methoxycarbonylanilino- (XVI; R = R′ = Me) or 2-*o*-carboxyanilino-4-methoxyquinazoline (XVI; R = H, R′ = Me) was heated. The observation that, under similar conditions, 2-*o*-methoxycarbonylanilino-4-*iso*propoxyquinazoline (XVI; R = Me, R′ = Pr^i) gave an *iso*propyl ether which was readily hydrolysed to the triazabenzanthracene (V) suggested that the *N*-methyl derivative, produced by thermal cyclisation, resulted from a rearrangement of an initially formed *O*-methyl ether. The triazabenzanthracene (V) could not be methylated with methyl iodide in acetone.



(XIV)



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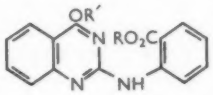
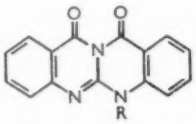


(XVI)



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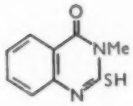

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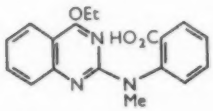
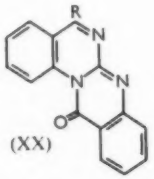
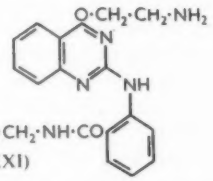


(XIX)



(XX)



(XXI)

A direct synthesis of the 7-methyltriazabenzanthracene (XV; R = Me) may be ambiguous, because the possibility of its isomerisation to a methylated triazanaphthacene (XVII; R = Me) cannot be excluded. The 6-methyl isomer (XIV; R = Me) cannot undergo such transformation into a methyltriazanaphthacene without intermediate demethylation or other equally improbable fissions of C–N bonds. This compound was synthesised and shown to be different from the original methylation product of the triazabenzanthracene (V), although, as expected, the ultraviolet absorption spectra of the two compounds were very similar (Table 1). Anthranilic acid and methyl *iso*thiocyanate furnished 3 : 4-dihydro-2-mercapto-3-methyl-4-oxoquinazoline (XVIII) which with methyl

iodide yielded a waxy methyl derivative. This evolved methanethiol in moist air and did not give satisfactory analytical results, but, when heated with methyl anthranilate, it yielded the 6-methyl derivative (XIV; R = Me).

Several projected syntheses of the 6-methyltriazabenzanthracene (XIV; R = Me) were unsuccessful because of the inaccessibility of starting materials. Thus 2-chloro-3 : 4-dihydro-3-methyl-4-oxoquinazoline could not be prepared by treatment of the corresponding 2-hydroxyquinazoline with phosphorus chlorides or thionyl chloride, by thermal rearrangement of 2-chloro-4-methoxyquinazoline, or by methylation of 2-chloro-4-hydroxyquinazoline. 2-Ethoxy-3 : 4-dihydro-3-methyl-4-oxoquinazoline, on being heated with methyl anthranilate, furnished only 3 : 4-dihydro-2-hydroxy-3-methyl-4-oxoquinazoline.

The triazanaphthacene (X) with methyl iodide and potassium carbonate in acetone readily gave a methyl derivative which was not demethylated by hydrobromic acid. That alkylation occurred at position 5 (XVII; R = Me) was shown by direct synthesis of the same compound by cyclisation of the hydrochloride of 2-*o*-carboxy-*N*-methylanilino-4-ethoxyquinazoline (XIX), itself prepared by interaction of 2-chloro-4-ethoxyquinazoline and *N*-methylanthranilic acid.

On methylation with methyl sulphate and sodium hydroxide, the triazanaphthacene (X) yielded the 5-methyl derivative (XVII; R = Me), the 7-methyltriazabenzanthracene (XV; R = Me), and the triazabenzanthracene (V). These isomerisations are most simply explained by assuming the intermediate formation of the guanidine (XI). Support for this was provided by the production of the hydrochloride of 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazoline (VI; R = H) when the triazanaphthacene (X) was dissolved in two equivalents of sodium hydroxide and a large excess of hydrochloric acid was added. Because of the behaviour of the triazabenzanthracene (V) towards sodium hydroxide, it is probable that the guanidine (XI) was involved in the analogous methylation of the triazabenzanthracene (V) with methyl sulphate.

Ethylation of the triazanaphthacene (X) in acetone with ethyl iodide and potassium carbonate occurred very slowly. The product was identical with one of two isomers formed by thermal cyclisation of 4-ethoxy-2-*o*-methoxycarbonylanilinoquinazoline (IV), and its light-absorption characters (Table 1) were so similar to those of the 7-methyltriazabenzanthracene (XV; R = Me), that it was considered to be the corresponding 7-ethyl derivative (XV; R = Et). Moreover, isomerisation of the product of direct ethylation of the triazanaphthacene (XVII; R = Et) is likely to produce only the 7-ethyltriazabenzanthracene (XV; R = Et). The similarity of the absorption spectrum of the second ethyl derivative (Table 1) formed by thermal cyclisation indicated its structure to be (XIV; R = Et).

Alkylation of the triazanaphthacene (X) with propyl, butyl, pentyl, hexyl, or benzyl halide was also slow; this observation together with the ultraviolet absorption spectra of the products (Table 1) led to the supposition that isomerisation had occurred and that these derivatives had the structures (XV; R = Alk or CH_2Ph). Attempts to alkylate or acylate the triazanaphthacene (X) with ethylene chlorohydrin, acetyl chloride, chloroacetyl chloride, benzoyl chloride, or ethyl chloroformate merely caused rearrangement to the triazabenzanthracene (V).

5-Chloro-12-oxo-12*H*-6 : 7 : 12a-triazabenz[*a*]anthracene (XX; R = Cl) was a readily hydrolysable compound prepared from the 5-oxo-derivative (V) and thionyl chloride. With sodium methoxide it gave 2-*o*-carboxyanilino-4-methoxyquinazoline (XVI; R = H, R′ = Me), the structure of which followed from the identity of its methyl ester (XVI; R = R′ = Me) with a specimen synthesised unequivocally from 2-chloro-4-methoxyquinazoline and methyl anthranilate. With sodium ethoxide, the chloro-compound (XX; R = Cl) gave a compound which had an ultraviolet absorption spectrum closely resembling that of 4-ethoxy-2-*o*-methoxycarbonylanilinoquinazoline (IV) (see Table 1), and which furnished the triazabenzanthracene (V) when heated with hydrobromic acid. It was considered to be the ester (XVI; R = R′ = Et).

XUM

The chloro-compound (XX; R = Cl) with simple aliphatic bases yielded mixtures which were not separated, but with piperidine and with morpholine, crystalline derivatives (XX; R = $C_5H_{10}N$ and C_4H_8ON, respectively) were obtained. Ethanolamine gave a compound, $C_{19}H_{21}O_3N_5$, containing one primary aliphatic amino-group and readily hydrolysable to the triazabenzanthracene (V). Since hydrolysis occurs readily with 4-alkoxyquinazolines, but not with 4-aminoquinazolines, this compound was evidently (XXI).

Experimental

2 : 4-*Dichloroquinazoline*.—The following procedure was more satisfactory than earlier methods.[2] 2 : 4-Dihydroxyquinazoline (20 g.) was heated with phosphoryl chloride (40 ml.) in a bath at 160° for 14 hr., or until the solid had dissolved completely. The hot mixture was poured on crushed ice (500 g.), and the precipitate, after being thoroughly washed with ice-water, was stirred with ether (700 ml.) for 3 hr. The ethereal solution was washed with N-sodium hydroxide and with water, dried ($MgSO_4$), and evaporated (yield, 21 g.), m. p. 116—118°.

4-*Ethoxy*-2-o-*methoxycarbonylanilinoquinazoline* (IV).—2-Chloro-4-ethoxyquinazoline [3] (4 g.) and methyl anthranilate (2·5 g.) in ethanol (30 ml.) were refluxed for 1 hr. The *base* (5·6 g.), precipitated by aqueous sodium carbonate, crystallised as prisms, m. p. 118—119°, from ethanol (Found: N, 13·3. $C_{18}H_{17}O_3N_3$ requires N, 13·0%). Its *picrate* crystallised from benzene as needles, m. p. 198° (decomp.) (Found: C, 52·4; H 4·1; N, 15·3. $C_{24}H_{20}O_{10}N_6$ requires C, 52·2; H, 3·7; N, 15·2%). The *hydrochloride*, precipitated from a benzene solution of the base, crystallised from ethanol; it had m. p. 172—173° (Found: C, 60·1; H, 5·1; N, 11·5. $C_{18}H_{18}O_3N_3Cl$ requires C, 60·1; H, 5·0; N, 11·7%).

Reactions of 4-*Ethoxy*-2-o-*methoxycarbonylanilinoquinazoline*.—(i) The solid which separated when the quinazoline (0·5 g.) in 5N-hydrochloric acid (7·5 ml.) was refluxed for 5 hr. was recrystallised from 2N-hydrochloric acid and gave 2-*amino*-3-o-*carboxyphenyl*-3 : 4-*dihydro*-4-*oxoquinazolinium chloride* (0·5 g.), m. p. 236—238° (Found: C, 56·7; H, 3·9; N, 13·0; Cl, 11·3. $C_{15}H_{12}O_3N_3Cl$ requires C, 56·7; H, 3·8; N, 13·2; Cl, 11·2%).

(ii) With 2N-hydrochloric acid and 30 minutes' heating, the insoluble material, after recrystallisation from 2-ethoxyethanol, gave 5 : 12-*dihydro*-5 : 12-*dioxo*-12H-6 : 7 : 12*a*-*triazabenz*[a]*anthracene* (39%), m. p. 254—256° (Found: C, 68·5; H, 3·2; N, 16·0. $C_{15}H_9O_2N_3$ requires C, 68·4; H, 3·5; N, 16·0%).

(iii) The quinazoline (0·5 g.) was boiled with concentrated hydrochloric acid (2 ml.) for 5 min. The triazabenzanthracene (0·1 g.), m. p. and mixed m. p. 255—256°, produced was separated from the hydrochloride of the starting material (0·16 g.) by extraction with 2-ethoxyethanol.

(iv) The solution obtained when the quinazoline (0·5 g.) was boiled for 30 min. with 2N-potassium hydroxide (10 ml.) was neutralised with acetic acid. Extraction of the gelatinous precipitate with 2-ethoxyethanol gave the triazabenzanthracene (0·05 g.), m. p. and mixed m. p. 255—255·5°. The gelatinous, amphoteric material furnished 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazolinium chloride, m. p. and mixed m. p. 236—238°, with concentrated hydrochloric acid.

(v) After 5 minutes' heating, a solid separated from a solution of the quinazoline (0·5 g.) in ethanol (10 ml.) containing potassium hydroxide (0·05 g.). An aqueous extract of the solid at pH 7 furnished 2-o-*carboxyanilino*-4-*ethoxyquinazoline* (0·1 g.), m. p. 200—201°, after recrystallisation from aqueous ethanol (Found: C, 65·6; H, 4·7; N, 13·9. $C_{17}H_{15}O_3N_3$ requires C, 66·0; H, 4·9; N, 13·6%). The water-insoluble fraction yielded on crystallisation from ethanol 4-*hydroxy*-2-o-*methoxycarbonylanilinoquinazoline* (0·05 g.), m. p. 290—294°, after sintering and turning yellow at 200—210° (Found: C, 65·1; H, 4·3; N, 14·1. $C_{16}H_{13}O_3N_3$ requires C, 65·1; H, 4·4; N, 14·2%).

4-*Hydroxy*-2-o-*methoxycarbonylanilinoquinazoline* (VIII).—2-Chloro-4-hydroxyquinazoline (2 g.) was heated in ethanol for 2 hr. with methyl anthranilate (1·7 g.). The product (2·6 g.) precipitated by aqueous sodium carbonate crystallised from ethanol as needles, m. p. and mixed m. p. 290—296°, after sintering and turning yellow at 200° and crystallising at 210—215° (Found: C, 65·5; H, 4·4. Calc. for $C_{16}H_{13}O_3N_3$: C, 65·1; H, 4·4%).

[2] Curd, Landquist, and Rose, *J.*, 1947, 775.
[3] Lange, Roush, and Asbeck, *J. Amer. Chem. Soc.*, 1930, **52**, 3696.

2-o-*Carboxyanilino-4-ethoxyquinazoline* (IX).—2-Chloro-4-ethoxyquinazoline (2 g.) and anthranilic acid (1·4 g.) were boiled in ethanol (20 ml.) for 90 min. The sodium salt precipitated when the mixture was poured into aqueous sodium carbonate furnished the free carboxylic acid as yellow prisms (1·2 g.), m. p. and mixed m. p. 200—201°, on crystallisation from aqueous ethanol containing 1% of acetic acid.

2-Amino-3-o-carboxyphenyl-3 : 4-dihydro-4-oxoquinazoline (VI; R = H).—5 : 6-Dihydro-5 : 12-dioxo-12*H*-6 : 7 : 12a-triazabenz[*a*]anthracene (1 g.) was heated with N-sodium hydroxide (7·7 ml.) for 15 min. Concentrated hydrochloric acid (30 ml.) was added to the filtered liquid at 0°; a solid separated and redissolved. The aminoquinazolinium chloride (0·8 g.) which crystallised slowly was recrystallised from 2N-hydrochloric acid; it had m. p. and mixed m. p. 236—238°.

Decomposition of this hydrochloride with ammonia gave the gelatinous, free amino-acid which with diazomethane in ether, afforded its *methyl ester* (VI; R = Me) (58%) as prisms (from ethanol) m. p. 224—225°, depressed to 195—200° on admixture with the isomeric 4-hydroxy-2-*o*-methoxycarbonylanilinoquinazoline (Found: C, 65·5; H, 4·6; N, 14·2. $C_{16}H_{13}O_3N_3$ requires C, 65·1; H, 4·4; N, 14·2%).

5 : 6-Dihydro-5 : 12-dioxo-12H-6 : 7 : 12a-triazabenz[a]*anthracene* (V).—(i) 2-*o*-Carboxyanilino-4-ethoxyquinazolinium chloride (1 g.), precipitated from a benzene solution of the base by hydrogen chloride, was heated at 130° for 1 hr. Ethyl chloride was evolved and the melt solidified. The triazabenzanthracene (0·58 g., 80%) was obtained as needles, m. p. and mixed m. p. 255—255·5°, by crystallisation of the melt from 2-ethoxyethanol.

(ii) 2-Chloro-4-hydroxyquinazoline (1 g.) and anthranilic acid (0·75 g.) were boiled in ethanol (10 ml.) for 1 hr. The hydrochloride (m. p. above 360°) which separated was unstable and could not be characterised; when boiled in water (10 ml.) for 10 min. it gave the triazabenzanthracene (1·12 g., 78%), m. p. and mixed m. p. 255—256°.

(iii) 2-Amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazoline, precipitated from a solution of its hydrochloride (4 g.) by ammonia, was dried by azeotropic distillation with benzene and heated at 200° for 4 min. Crystallisation of the product from 2-ethoxyethanol furnished the triazabenzanthracene (3·2 g., 97%), m. p. and mixed m. p. 255—256°.

(iv) The methyl ester of this 2-aminoquinazoline was heated at 255° for 2 hr. Recrystallisation of the resulting melt from 2-ethoxyethanol afforded the triazabenzanthracene in 88% yield.

Cyclisation of 4-Hydroxy-2-o-methoxycarbonylanilinoquinazoline.—(i) This ester (20 g.) on being heated at 255° for 2 hr. afforded yellow crystals which by fractional crystallisation from 2-ethoxyethanol and dimethylformamide were separated into the triazabenzanthracene (9·6 g.), m. p. and mixed m. p. 255—256°, and 11 : 12-*dihydro*-11 : 12-*dioxo*-5H-5 : 6 : 11*a-triazanaphthacene* (X) (3·8 g.), yellow prisms, m. p. 359—362° (Found: C, 68·7; H, 3·3; N, 15·8. $C_{15}H_9O_2N_3$ requires C, 68·4; H, 3·5; N, 16·0%).

(ii) The solid produced when this ester (30 g.) was boiled in 2N-hydrochloric acid (300 ml.) for 2 hr. gave the triazabenzanthracene (23 g., 85%) on crystallisation from 2-ethoxyethanol.

Degradation of the Triazabenzanthracene (V).—(i) A solution of the triazabenzanthracene (12 g.) in boiling 2N-sodium hydroxide (44 ml.) was evaporated to dryness. The residue, mixed with copper bronze (2 g.), was refluxed in quinoline (10 ml.) for 3 hr. After removal of the quinoline in steam, *NN'*-diphenylguanidine (0·77 g.) was collected in ether, recovered and crystallised from ethanol; it had m. p. 146—148° undepressed by an authentic specimen.[4]

(ii) The triazabenzanthracene (1 g.) was boiled for 30 min. with 0·1N-sodium hydroxide (37 ml., 1 equiv.). The alkali-insoluble material (0·48 g.) was unchanged triazabenzanthracene. Addition of hydrochloric acid (*d* 1·18) to the concentrated alkaline filtrate furnished 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazolinium chloride (0·51 g., 42%), m. p. and mixed m. p. 236—238°.

Reaction of 2-Chloro-4-ethoxyquinazoline with Methyl Anthranilate.—2-Chloro-4-ethoxyquinazoline (5 g.) and methyl anthranilate (3·6 g.) were heated at 112°. After the exothermic phase of the reaction and the evolution of ethyl chloride (40 min.), the solid produced gave as an ethanol-soluble fraction 4-hydroxy-2-*o*-methoxycarbonylanilinoquinazoline (1·9 g.), m. p. and mixed m. p. 290—296° after sintering at 210—215°, and, as an ethanol-insoluble fraction, the triazabenzanthracene (V) (2·9 g.), m. p. and mixed m. p. 255—255·5°.

[4] Partridge and Turner, *J. Pharm. Pharmacol.*, 1953, **5**, 103.

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From a sample removed from the reaction mixture after 10 minutes' heating, 4-ethoxy-2-*o*-methoxycarbonylanilinoquinazolinium chloride, m. p. and mixed m. p. 172—173°, was isolated. This hydrochloride (2 g.) was heated at 130° for 30 min. Fractionation of the cooled melt with ethanol again furnished 4-hydroxy-2-*o*-methoxycarbonylanilinoquinazoline (0·4 g.) and the triazabenzanthracene (1 g.).

Interconversion of the Triazabenzanthracene (V) *and the Triazanaphthacene* (X).—(i) A solution of the triazabenzanthracene (10 g.) in concentrated sulphuric acid (30 ml.) was kept at 50° for 20 min. and then poured into anhydrous methanol (150 ml.); this gave a white solid which in contact with water turned yellow and on crystallisation from dimethylformamide furnished the triazanaphthacene (3·8 g.), m. p. and mixed m. p. 358—360°. The methanolic mother-liquor was concentrated to a small volume and diluted with water. From the resulting precipitate were obtained: (*a*) an ethanol-soluble fraction, 4-hydroxy-2-*o*-methoxycarbonylanilinoquinazoline (4·3 g.), m. p. and mixed m. p. 290—296° after sintering at 195—200°, and (*b*) an ethanol-insoluble fraction, the triazabenzanthracene (1·6 g.), m. p. and mixed m. p. 255—256°.

(ii) The yellow solid obtained when a solution of the triazabenzanthracene (10 g.) in concentrated sulphuric acid (30 ml.) was poured on crushed ice afforded the triazabenzanthracene (5·5 g.) and, as a fraction insoluble in 2-ethoxyethanol, the triazanaphthacene (2·6 g.).

(iii) The triazanaphthacene (0·5 g.) was treated with concentrated sulphuric acid (5 ml.) as described for the triazabenzanthracene. The products isolated when the solution was poured into methanol were the triazabenzanthracene (0·1 g.), the triazanaphthacene (0·185 g.), and 4-hydroxy-2-*o*-methoxycarbonylanilinoquinazoline (0·2 g.).

(iv) A suspension of the triazanaphthacene (1 g.) in 2-ethoxyethanol (20 ml.) was boiled for 24 hr.; the yellow colour gradually disappeared and the colourless solution deposited the triazabenzanthracene (0·95 g.).

4-*Methoxy*-2-*o*-*methoxycarbonylanilinoquinazoline* (XVI; R = R′ = Me) was precipitated (1·4 g.) when the solution obtained by refluxing 2-chloro-4-methoxyquinazoline [2] (0·9 g.) and methyl anthranilate (0·6 ml.) in ethanol (10 ml.) was poured into aqueous sodium carbonate; it formed needles, m. p. 128—129°, from ethanol (Found: C, 66·2; H, 4·7; N, 13·8. $C_{17}H_{15}O_3N_3$ requires C, 66·0; H, 4·9; N, 13·6%). Its *picrate*, needles from ethanol, had m. p. 176—178° (Found: N, 15·9. $C_{23}H_{18}O_{10}N_6$ requires N, 15·6%).

5 : 6-*Dihydro*-7-*methyl*-5 : 12-*dioxo*-12H-6 : 7 : 12*a*-*triazabenzanthracene* (XV; R = Me).—(i) The triazabenzanthracene (V) (5 g.) in 5N-sodium hydroxide (20 ml.) was treated with methyl sulphate (3 ml.) during 10 hr. Neutralisation of the reaction mixture gave the 7-*methyl derivative* (1·9 g.), which crystallised from ethanol as needles, m. p. 165—166° (Found: C, 69·2; H, 3·7; N, 15·2. $C_{16}H_{11}O_2N_3$ requires C, 69·3; H, 4·0; N, 15·2%).

(ii) 4-Methoxy-2-*o*-methoxycarbonylanilinoquinazoline (0·5 g.) was heated at 255° for 2 hr. Crystallisation of the product from ethanol yielded the same 7-methyltriazabenzanthracene (0·72 g.), m. p. and mixed m. p. 165—166°.

(iii) 2-*o*-Carboxyanilino-4-methoxyquinazoline (1·5 g.) when heated at 250° for 6 hr. gave the 7-methyltriazabenzanthracene (0·48 g.), m. p. and mixed m. p. 165—166°, after crystallisation from ethanol.

This compound was recovered after an attempted demethylation with 48% hydrobromic acid.

2-*Chloro*-4-iso*propoxyquinazoline*.—2 : 4-Dichloroquinazoline (20 g.) was heated at 40° for 30 min. with sodium (2·3 g.) in propan-2-ol (100 ml.). The iso*propyl ether* (9·8 g.) crystallised slowly from the oil precipitated by dilution of the mixture with water; it formed lustrous plates, m. p. 47—48°, from aqueous methanol (Found: N, 12·7. $C_{11}H_{11}ON_2Cl$ requires N, 12·6%).

2-*o*-*Methoxycarbonylanilino*-4-iso*propoxyquinazoline* (XVI; R = Me, R′ = Pr^i).—2-Chloro-4-*iso*propoxyquinazoline (1 g.) and methyl anthranilate (0·6 ml.) were refluxed in ethanol (10 ml.) for 3 hr. The *base* (1·2 g.) precipitated by aqueous sodium carbonate crystallised from aqueous ethanol as needles, m. p. 91—92° (Found: C, 68·0; H, 5·5; N, 12·4. $C_{19}H_{19}O_3N_3$ requires C, 67·6; H, 5·7; N, 12·5%). Its *picrate* (needles from benzene) had m. p. 196—197° (decomp.) (Found: C, 53·1; H, 3·9; N, 14·9. $C_{25}H_{22}O_{10}N_6$ requires C, 53·0; H, 3·9; N, 14·8%).

iso*Propoxy*-12-*oxo*-12H-6 : 7 : 12*a*-*triazabenz*[a]*anthracene*.—2-*o*-Methoxycarbonylanilino-4-*iso*propoxyquinazoline (4 g.), after being heated at 250° for 5 hr., was extracted with benzene. The benzene-insoluble fraction after recrystallisation from 2-ethoxyethanol yielded the triazabenzanthracene (V) (0·25 g.). An ethereal solution of the benzene-soluble material, by

fractional precipitation with light petroleum and repeated filtration through charcoal and kieselguhr, gave the iso*propyl ether* (0·43 g.) as yellow needles, m. p. 85—88° (Found: C, 70·6; H, 4·9; N, 13·5. $C_{18}H_{15}O_2N_3$ requires C, 70·8; H, 5·0; N, 13·8%).

When boiled with 2N-hydrochloric acid (3 ml.) for 30 min., this ether (0·1 g.) gave the triazabenzanthracene (V) (0·065 g.), m. p. and mixed m. p. 255—256°.

3 : 4-*Dihydro*-2-*mercapto*-3-*methyl*-4-*oxoquinazoline* (XVIII).—Anthranilic acid (2 g.), methyl *iso*thiocyanate (1 g.), and acetic acid (6 ml.) were heated in a sealed tube at 150° for 90 min. The solid which crystallised gave the pure *thiol* (1·1 g.) on crystallisation from ethanol and then from acetic acid; this formed yellow prisms, m. p. 260—261° (Found: C, 56·5; H, 4·2; S, 16·4. $C_9H_8ON_2S$ requires C, 56·3; H, 4·2; S, 16·6%).

5 : 6-*Dihydro*-6-*methyl*-5 : 12-*dioxo*-12H-6 : 7 : 12*a*-*triazabenz*[a]*anthracene* (XIV; R = Me).—The foregoing thiol (20 g.) in dry acetone (150 ml.) was refluxed with methyl iodide (10 ml.) for 10 hr. After isolation the product was distilled at 138—142°/0·5—0·7 mm. and had m. p. 57—58°. No satisfactory analytical results were obtained. The redistilled material (18 g.) and methyl anthranilate (14·5 g.) were heated at 255° for 5 hr. After removal of basic material with dilute acid, the residue, on repeated crystallisation from ethanol, gave the 6-*methyl derivative* (6 g.) as needles, m. p. 175—176°, depressed to 165—172° by the 7-methyl isomer (Found: C, 69·0; H, 3·9; N, 15·2. $C_{16}H_{11}O_2N_3$ requires C, 69·3; H, 4·0; N, 15·2%).

2-*o*-Carboxy-*N*-methylanilino-4-ethoxyquinazoline (XIX) was formed as its *hydrochloride* (11 g.) when *N*-methylanthranilic acid (7·5 g.) and 2-chloro-4-ethoxyquinazoline (10 g.) were boiled in ethanol (100 ml.) for 2 hr. and the solution was evaporated. It crystallised from 2N-hydrochloric acid as needles, m. p. 143—144° (Found: N, 11·6; Cl, 10·1. $C_{18}H_{18}O_3N_3Cl$ requires N, 11·7; Cl, 9·9%). The free *base*, m. p. 66—68°, could not be recrystallised; it had $\lambda_{max.}$ 235, 277 mμ (ε 36,800, 16,300, respectively) (Found: C, 66·4; H, 5·1; N, 12·7. $C_{18}H_{17}O_3N_3$ requires C, 66·9; H, 5·3; N, 13·0%).

11 : 12-*Dihydro*-5-*methyl*-11 : 12-*dioxo*-5H-5 : 6 : 11*a*-*triazanaphthacene* (XVII; R = Me).—2-*o*-Carboxy-*N*-methylanilino-4-ethoxyquinazolinium chloride (3 g.) was heated at 255° for 2 hr.; ethyl chloride was evolved. Crystallisation of the cooled melt from benzene furnished the 5-*methyltriazanaphthacene* (1·35 g.) as needles, m. p. 283—284° (Found: C, 69·0; H, 4·2; N, 14·9. $C_{16}H_{11}O_2N_3$ requires C, 69·3; H, 4·0; N, 15·2%).

Methylation of the Triazanaphthacene (X).—(i) The triazanaphthacene (0·5 g.) in dry acetone (20 ml.) was boiled for 4 hr. with methyl iodide (0·2 ml.) and potassium carbonate (0·1 g.). The product (0·47 g.) crystallised from benzene and had m. p. 283—284°, undepressed by the foregoing 5-methyltriazanaphthacene.

(ii) The solution resulting from the treatment of the triazanaphthacene (3 g.) in 2N-sodium hydroxide (15 ml.) with methyl sulphate (0·6 ml.) for 8 hr. was neutralised. 2-Ethoxyethanol extracted from the precipitate the triazabenzanthracene (V) (0·36 g.), m. p. and mixed m. p. 255—255·5°. Dilution of the mother-liquor with water gave a precipitate from which the 5-methyltriazanaphthacene (XVII; R = Me) (1·1 g.), m. p. and mixed m. p. 283—284°, was obtained by crystallisation from ethanol. On the addition of water to the ethanol mother-liquor, the 7-methyltriazabenzanthracene (XV; R = Me) (0·48 g.), m. p. and mixed m. p. 165—166°, crystallised. The 2-ethoxyethanol-insoluble solid was the triazanaphthacene (0·24 g.).

The 5-methyltriazanaphthacene was recovered after being boiled with 48% hydrobromic acid for 2 hr.

Degradation of the Triazanaphthacene (X).—A solution prepared by boiling the triazanaphthacene (0·5 g.) with 2N-sodium hydroxide (20 ml.) for 30 min. was concentrated to 10 ml., mixed with concentrated hydrochloric acid (10 ml.), and kept at 0° overnight. After recrystallisation from 2N-hydrochloric acid, the product (0·35 g.) had m. p. 236—238°, undepressed by 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazolinium chloride.

7-*Ethyl*-5 : 6-*dihydro*-5 : 12-*dioxo*-12H-6 : 7 : 12*a*-*triazabenz*[a]*anthracene* (XV; R = Et).—The triazanaphthacene (X) (0·7 g.) in dry acetone (15 ml.) was boiled for 24 hr. with potassum carbonate (0·1 g.) and ethyl iodide (0·3 ml.). The *ethyl derivative* (0·29 g., 39%) crystallised from ethanol as solvated needles, m. p. 166—168° (Found, on dried material: C, 69·8; H, 4·6; N, 14·4. $C_{17}H_{13}O_2N_3$ requires C, 70·1; H, 4·5; N, 14·4%).

The following 7-substituted-5 : 6-dihydro-5 : 12-dioxo-12*H*-6 : 7 : 12a-triazabenz[*a*]anthracenes were similarly prepared from the triazanaphthacene (X): 7-*Propyl*, needles from ethanol, m. p. 155—156° (Found: N, 13·6. $C_{18}H_{15}O_2N_3$ requires N, 13·8%); yield 35%. 7-*Butyl*,

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needles from ethanol, decomposed at 180—190° without melting (Found: N, 13·3. $C_{19}H_{17}O_2N_3$ requires N, 13·2%); yield 58%. **7-*Pentyl***, needles from ethanol, decomposed at 180—190° without melting (Found: N, 12·5. $C_{20}H_{19}O_2N_3$ requires N, 12·6%); yield 44%. **7-*Hexyl***, needles from ethanol, decomposed at 180—190° without melting (Found: N, 12·0. $C_{21}H_{21}O_2N_3$ requires N, 12·1%); yield 76%. **7-*Benzyl***, yellow needles from ethanol, m. p. 189—191° (Found: N, 12·3. $C_{22}H_{15}O_2N_3$ requires N, 11·9%); yield 51%.

Cyclisation of **4-*Ethoxy*-2-*o*-*methoxycarbonylanilinoquinazoline***.—This quinazoline (10 g.) was heated at 255° for 10 hr. The fraction of the product insoluble in hot ethanol gave on crystallisation from benzene–light petroleum the 7-ethyltriazabenzanthracene (XV; R = Et) (1 g.), m. p. and mixed m. p. 166—168° (Found: C, 69·9; H, 4·4; N, 14·5. Calc. for $C_{17}H_{13}O_2N_3$: C, 70·1; H, 4·5; N, 14·4%). The hot ethanol-soluble fraction (6 g., m. p. 135°) furnished the ***6-ethyl isomer*** (XIV; R = Et), m. p. 135—136°, after recrystallisation from light petroleum (Found: C, 70·2; H, 4·9; N, 14·6. $C_{17}H_{13}O_2N_3$ requires C, 70·1; H, 4·5; N, 14·4%).

Both the foregoing compounds were stable to 48% hydrobromic acid.

5-*Chloro*-12-*oxo*-12H-6 : 7 : 12*a*-*triazabenz*[a]*anthracene* (XX; R = Cl).—The triazabenzanthracene (V) (0·5 g.) was refluxed with thionyl chloride (10 ml.) for 3 hr. After removal of excess of reagent, the ***5-chloro-derivative*** (0·35 g.) was sublimed at 150°/0·01 mm., forming bright yellow prisms, m. p. 191—192° (Found: C, 63·8; H, 3·0; N, 14·9; Cl, 12·8. $C_{15}H_8ON_3Cl$ requires C, 64·0; H, 2·8; N, 14·9; Cl, 12·6%). This compound was readily hydrolysed in moist air to the triazabenzanthracene (V).

2-*o*-*Carboxyanilino*-4-*methoxyquinazoline* (XVI; R = H, R′ = Me).—To the above, freshly prepared 5-chloro-derivative (1 g.) was added sodium ethoxide [from sodium (0·15 g.)] in dry methanol (20 ml.), and the mixture was shaken until the solid had dissolved, neutralised, and poured into water (200 ml.). The precipitated oil, which solidified when warmed, afforded ***2-o-carboxyanilino-4-methoxyquinazoline*** (0·7 g.) as needles, m. p. 120—121°, on crystallisation from methanol; $\lambda_{max.}$ 248, 282, 291, 341 mμ (ε 20,300, 23,300, 25,400, 14,400, respectively) (Found: C, 65·0; H, 4·3; N, 14·1. $C_{16}H_{13}O_3N_3$ requires C, 65·1; H, 4·4; N, 14·2%).

An ethanol solution of this compound yielded with diazomethane 4-methoxy-2-*o*-methoxycarbonylanilinoquinazoline (76%), m. p. and mixed m. p. 128—128·5°. On being heated with 48% hydrobromic acid, it gave the triazabenzanthracene (V) and 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazoline which was characterised as its hydrochloride, m. p. and mixed m. p. 236—238°.

4-*Ethoxy*-2-*o*-*ethoxycarbonylanilinoquinazoline* (XVI; R = R′ = Et) was obtained by treatment of the 5-chlorotriazabenzanthracene (1·1 g.) with sodium ethoxide [from sodium (0·2 g.)] in ethanol (25 ml.) in a similar way and crystallised from methanol forming needles (0·49 g.), m. p. 104—105°; $\lambda_{max.}$ 251, 291, 342 mμ (ε 15,800, 26,600, 15,100, respectively) (Found: C, 67·4; H, 5·4; N, 12·4. $C_{19}H_{19}O_3N_3$ requires C, 67·6; H, 5·7; N, 12·5%). It yielded the same products as the foregoing compound on treatment with 48% hydrobromic acid. On being refluxed with 2·5N-sodium hydroxide (7 ml.), this compound (0·1 g.) afforded, after addition of excess of concentrated hydrochloric acid, 2-amino-3-*o*-carboxyphenyl-3 : 4-dihydro-4-oxoquinazolinium chloride (0·065 g.).

12-*Oxo*-5-*piperidino*-12H-6 : 7 : 12*a*-*triazabenz*[a]*anthracene* (XX; R = $C_5H_{10}N$).—The 5-chlorotriazabenzanthracene (8·5 g.) and dry piperidine (30 ml.) were shaken for 30 min., warmed to 60°, and poured into water (250 ml.). A solution of the precipitated resin in 2N-hydrochloric acid (30 ml.) was treated fractionally with aqueous ammonia and repeatedly filtered through charcoal and kieselguhr. The final fractions (3·6 g.) furnished the pure ***piperidino-derivative*** m. p. 205—206° (from ether); $\lambda_{max.}$ 245, 269, 311, 360, 405 mμ (ε 31,000, 22,000, 22,000, 19,000, 10,200, 3500, respectively) (Found: C, 72·4; H, 5·1; N, 16·7. $C_{20}H_{18}ON_4$ requires C, 72·7; H, 5·5; N, 17·0%). Its ***picrate*** crystallised from ethanol as prisms, m. p. 220—221° (decomp.) (Found: C, 55·8; H, 3·8; N, 17·8. $C_{26}H_{21}O_8N_7$ requires C, 55·8; H, 3·8; N, 17·5%).

5-*Morpholino*-12-*oxo*-12H-6 : 7 : 12*a*-*triazabenz*[a]*anthracene* (XX; R = C_4H_8ON), prepared in a similar manner, crystallised from light petroleum (b. p. 100—120°) as yellow needles, m. p. 230—232°; $\lambda_{max.}$ 242, 265, 313, 365 mμ (ε 31,000, 22,000, 18,000, 10,000, respectively) (Found: C, 68·3; H, 4·6; N, 16·4. $C_{19}H_{16}O_2N_4$ requires C, 68·7; H, 4·9; N, 16·9%). The ***picrate*** (prisms from ethanol) had m. p. 246—247° (Found: C, 53·3; H, 3·4; N, 17·3. $C_{25}H_{19}O_9N_7$ requires C, 53·5; H, 3·4; N, 17·5%).

4-2′-*Aminoethoxy*-2-(*o*-N-2′-*hydroxyethylcarbamoylanilino*)*quinazoline* (XXI).—The 5-chlorotriazabenzanthracene (1 g.) was brought into reaction with sodium (0·09 g.) in dry ethanolamine

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(10 ml.). The *amide* (0·75 g.), precipitated by water, crystallised from ethanol as yellow needles, m. p. 207—208° (Found: C, 62·4; H, 6·1; N, 18·8; NH_2, 4·5, 4·0, 4·3. $C_{19}H_{19}O_3N_4{\cdot}NH_2$ requires C, 62·1; H, 5·8; N, 19·0; NH_2, 4·4%). The *picrate* crystallised as prisms, m. p. 184—185°, from ethanol (Found: C, 50·5; H, 4·2; N, 18·3. $C_{25}H_{24}O_{10}N_8$ requires C, 50·3; H, 4·0; N, 18·8%).

THE UNIVERSITY, NOTTINGHAM. [*Received, November 5th*, 1958.]

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294. *Some Properties of, and a Structural Scheme for, the Harmotome Zeolites.*

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An account is given of dehydration, sorption, and *X*-ray diffraction for several closely-related synthetic aluminosilicates belonging to the harmotome–phillipsite group of zeolites. A structure is proposed for a cubic variety of the synthetic phases, and the relations between this structure and orthorhombic or monoclinic unit cells of harmotome and phillipsite are indicated. The aluminosilicate framework of the cubic structure is formed by placing cubic structural units at each corner and at the centre of each unit cell. These cubic units, which occur also in Linde Sieve A,[1] are formed by union by oxygen bridges of two rings of four SiO_4 or AlO_4 tetrahedra, giving a cluster of eight such tetrahedra. Each cubic unit is then joined by single oxygen bridges to eight similar units, and thereby a system of intersecting channels with eight-membered rings as "windows" is produced.

HARMOTOME, phillipsite, and wellsite are three closely related natural zeolites, harmotome and phillipsite being of fairly widespread occurrence whereas wellsite is rare. Several synthetic minerals have been observed in the calcium, barium, potassium, and sodium aluminosilicate crystallisation fields which bear marked similarities to these natural minerals.[2-5] A structure is now proposed for a synthetic cubic form of the sodium minerals referred to as Species Na-*P* in an earlier paper.[2] This structure, with slight modifications, could also fit the symmetry of tetragonal and orthorhombic sodium forms and, although they differ greatly in symmetry from the cubic mineral, it is shown that the natural minerals may have a closely similar aluminosilicate framework. Dehydration, sorption, and ion exchange were also investigated for the synthetic sodium minerals.

EXPERIMENTAL

The method of mineral synthesis has been described.[2] *X*-Ray powder data were obtained with a 9 cm. Debye–Scherrer camera and a Guinier camera, and single-crystal diffraction patterns for natural harmotome were obtained with a Weissenberg camera and a Unicam single-crystal goniometer. Cu-K_α radiation was used throughout. Dehydration was studied thermogravimetrically by heating to constant weight in a furnace a known weight of the zeolite contained in a Morgan ΔRR alumina crucible, which was suspended from one of the pans of a modified beam balance by a platinum wire. The standard gas volumetric method was used in sorption work.

Finally, ion-exchanged forms of several of the species, natural or synthetic, were prepared by heating the mineral in sealed Pyrex tubes with the appropriate chlorides in aqueous saturated solution at 100°. In all, three treatments were given lasting for a total of 15 hr. for the synthetic minerals. The natural minerals were treated until the mother liquor gave no trace of calcium or barium.

[1] Reed and Breck, *J. Amer. Chem. Soc.*, 1956, **78**, 5972; Barrer and Meier, *Trans. Faraday Soc.*, 1958, **54**, 1074.
[2] Barrer, Baynham, Bultitude, and Meier, *J.*, 1959, 195.
[3] Barrer and Baynham, *J.*, 1956, 2882.
[4] Barrer, Hinds, and White, *J.*, 1953, 1466.
[5] Barrer, unpublished work.

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Ion-exchange and X-Ray Powder Patterns.—Three zeolitic sodium aluminosilicate phases designated Na-*P* have previously been prepared, all of which belong to the harmotome family of zeolites.[2] These comprise a cubic phase which may be called Na-*P*1, a tetragonal phase Na-*P*2, and an orthorhombic phase Na-*P*3. The powder photographs are shown in the Plate. From the cubic variety, Na-*P*1, the Li^+-, K^+-, Ca^{2+}-, and Ba^{2+}-exchanged forms were prepared. All exhibited slight changes from cubic symmetry, having the strong (211) line split into two, while in the Ca^{2+}- and K^+-forms the very strong (310) line was also doubled. It was however possible to index the forms to cubic pseudo-cells having the values of a: Li^+ $9{\cdot}8_9$, Na^+ $10{\cdot}0_1$, K^+ $9{\cdot}8_3$, Ca^{2+} $9{\cdot}9_5$, Ba^{2+} $10{\cdot}0_3$ Å.

From the tetragonal form, Na-*P*2, the Ca^{2+}- and Ba^{2+}-exchanged forms were also prepared. The powder patterns differed from the corresponding patterns of these forms derived from

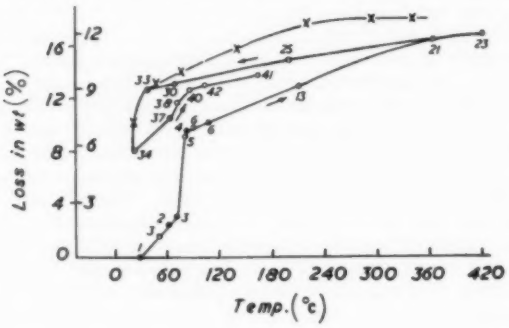

FIG. 1. *Dehydration curves of* Na-*P on the thermogravimetric balance* (○, ●) *and under vacuum conditions* (×). The inner left-hand scale is the number of water molecules lost per unit cell.

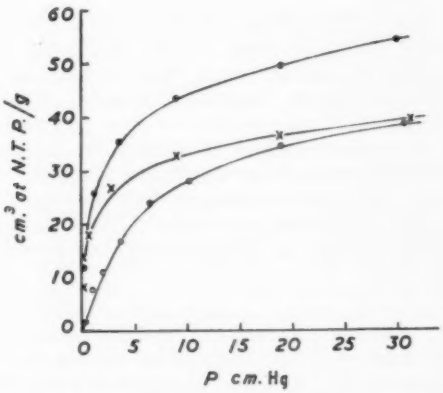

FIG. 2. *Sorption of ammonia at* 210° *on species exchanged derivatives.* Na-*P* (○) *and its* Ca- (●) *and* Ba- (×) forms.

Na-*P*1. They showed even more marked similarities to the patterns of natural minerals of the harmotome group than did the same ion-exchanged forms of Na-*P*1, or the parent phases Na-*P*1 and Na-*P*2 (Table 3 and Plate). These Ca^{2+}- and Ba^{2+}-forms contained respectively 19·9% and 14·7% by weight of water compared with 17·0% for the original sodium form.

Also shown in the Plate for comparison are powder photographs of natural harmotome, its Na^+-exchanged form, a new natural zeolite of the harmotome family, found in Co. Down, Ireland, and provisionally named garronite by its discoverer,[6] Dr. G. Walker (Geology Department, Imperial College), and a synthetic phase designated K-*M*.[3]

Dehydration.—On dehydration of Na-*P* below 73°, several hours were required before the end points were reached, but between 73° and 83° a marked step was observed in the curve, 3 days being required to reach the end points over this portion of the curve. Above 83° and below 73° the curve was continuous. This portion of the curve is represented by points 1 to 23 in Fig. 1 (○), only a few of the observed points being included. On rehydration, after heating the crystals to ~450°, an apparent hysteresis phenomenon occurred (points 23 to 34, Fig. 1).

[6] Walker, personal communication.

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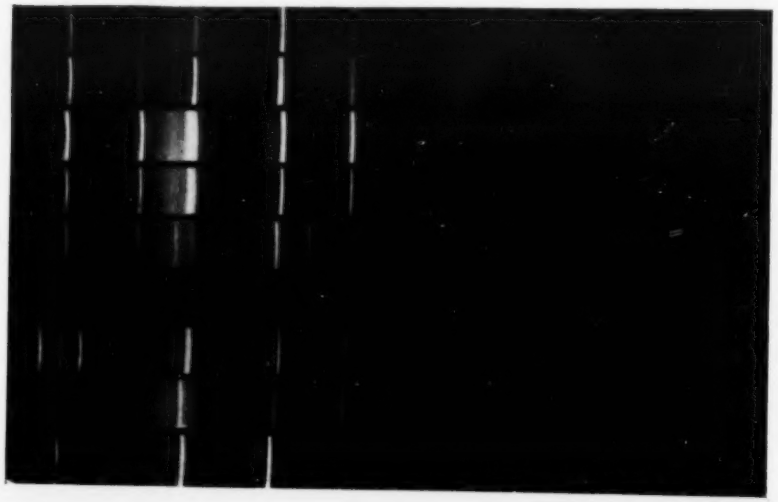
Comparative X-ray powder photographs of a series of zeolites of the harmotome family.



1. Na-*P*1 (cubic).
2. Na-*P*2 (tetragonal).
3. Ca-exchanged Na-*P*2.
4. New naturally occurring zeolite, garronite.[14]
5. Na-*P*3 (orthorhombic).
6. Species K-*M*.[10]
7. Natural harmotome.
8. Ba-exchanged Na-*P*2.
9. Na-exchanged phase from natural harmotome.

[*To face p.* 1522.

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This may be due to very slow attainment of equilibrium but no trend with time was noticeable, some readings being taken after 3 hr. and others after 20 hr. About four days elapsed between the readings at 79° and 57° for a gain in weight of 0·1%. After three weeks at room temperature an ~4½% gain in weight had been recorded. On reheating, the curve did not return to its original position (points 34 to 42, Fig. 1). A second sample (●), on dehydration, gave the same step in the curve, this sample being heated to a maximum temperature of 108°. On cooling to room temperature it had regained its original weight within six days.

A smooth curve was obtained on dehydrating a specimen under vacuum (*X*) for 16 hr. at increasing temperatures (see Fig. 1). Almost two-thirds of the water was removed by evacuating the sample at room temperature. After the fully dehydrated sample had been exposed to the atmosphere at room temperature for four weeks, a weight of water had been regained equal only to that removed above room temperature, *i.e.*, about one third.

Heating of samples to 61° and 90° caused a slight decrease in the unit cell from $10{\cdot}0_1$ Å to $9{\cdot}9_5$ Å with practically no alteration in the diffraction intensities. At 165° and 260° the cell edge showed a decrease in size of ~5½% to $9{\cdot}4_6$ Å, with a marked alteration in some of the intensities. Thus (200), (222), and (330) lines became stronger and the (310) and (321) weaker, and there appeared in addition some reflections for which $h + k + l = 2n + 1$. After standing over a saturated ammonium chloride solution for about three weeks the unit cell and diffraction-line intensities had returned to those of the original mineral except for the appearance of a weak (111) reflection. Samples heated to 450° under vacuum appeared to have been destroyed.

Sorption.—Since outgassing under vacuum at 450° appeared to have destroyed the material, dehydration for sorption experiments was carried out at between 200° and 300° for 16 hr. The sodium form sorbed no appreciable amount of oxygen at −183° and sorption of ammonia by the sodium, barium, and calcium ionic species was very slow both at room temperature and at 100°, but at 210° apparent equilibrium was reached after 24 hr. The sodium and barium forms sorbed, per g. of original hydrated material, almost 40 c.c. of ammonia at N.T.P. at 30 cm. pressure, and the calcium form ~55 c.c. under the same conditions (Fig. 2). A specimen of natural harmotome from Strontian, Argyllshire, outgassed at 180° for 16 hr. also sorbed no oxygen at −183° and ammonia slowly at room temperature. Per gram of the original hydrated mineral, 27·2 c.c. at N.T.P. of ammonia were sorbed after 14 hr.

Composition of Potassium and Calcium Derivatives.—Other synthetic minerals with a similar type of framework structure have been observed in the potassium, calcium, and barium aluminosilicate fields.[3] The potassium analogue was of widespread occurrence, being grown from gels $K_2O,Al_2O_3,nSiO_2,xH_2O$ where $n = 1$—7 over a range of 200° to 300° with excess of potassium hydroxide present, and at slightly lower temperatures from gels $n = 7$—10. This compares with growth of Na-*P*[2] from gels of composition $Na_2O,Al_2O_3,nSiO_2,xH_2O$ where $n = 1$—12 in presence of excess of sodium hydroxide over a range of 60° to 250°. The *X*-ray pattern of the potassium mineral (K-*M*), which was also prepared as an alteration product of leucite by treatment with potassium hydroxide at 200—250°,[4] was very close to the orthorhombic sodium form grown at 250° (Plate). The composition of the potassium mineral was always near to $K_2O,Al_2O_3,3SiO_2,3H_2O$.

A synthetic calcium " harmotome " was grown from a gel $CaO,Al_2O_3,4SiO_2,xH_2O$ by treatment for long periods between 200° and 300°.[5] The product contained excess of calcium oxide, possibly as free lime, and analysis gave $1\frac{1}{2}CaO,Al_2O_3,3{\cdot}3SiO_2,1\frac{1}{2}H_2O$. A barium harmotome-like mineral was grown from a parent gel $BaO,Al_2O_3,3SiO_2$ with excess of $Ba(OH)_2$, pH ~ 10·5, by heating for two days at 220° and then three days at 200°; and from a similar gel with no excess of $Ba(OH)_2$, pH ~ 7·0, by heating for three days at 360°.[5]

A natural mineral very similar to one of the synthetic species is garronite. From its crystal habit it was classified by Dr. G. Walker as probably belonging to the harmotome group of minerals although identical with none of them.[6] The *X*-ray pattern, which can be indexed to the tetragonal system with $a = 10{\cdot}0_1$ Å and $c = 9{\cdot}8_7$ Å, is almost exactly the same as that of a calcium-exchanged tetragonal form of species Na-*P* (cf. Table 3 and Plate). No analysis of garronite is available, but it seems clear that it is also a zeolite of the harmotome group based on a similar aluminosilicate framework to that of the natural and synthetic phases already discussed.

Crystal Symmetry and a Suggested Structure for Species Na-*P*.—As seen from Table 1, there is no obvious relationship between the crystal symmetry and the composition of the several phases, collectively designated as Na-*P*, which varies from an $Al_2O_3 : SiO_2$ ratio of 1 : 3·35 to

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one of 1 : 5·26. The density of sample 4, Table 1, was found to be ~2·08 g./c.c. by successive suspensions in liquid mixtures (methylene iodide–benzene) of known density. Hence the number of aluminium and silicon atoms per unit cell was found to be 5·3 and 10·4 respectively. Since the unit cell must contain an integral number of oxygen and (Al + Si) atoms,[7] this gives 16(Al + Si) and 32 oxygen atoms per unit cell. The *X*-ray powder data [2] are, except for a very weak (410) line, consistent with a body-centred cubic unit cell.

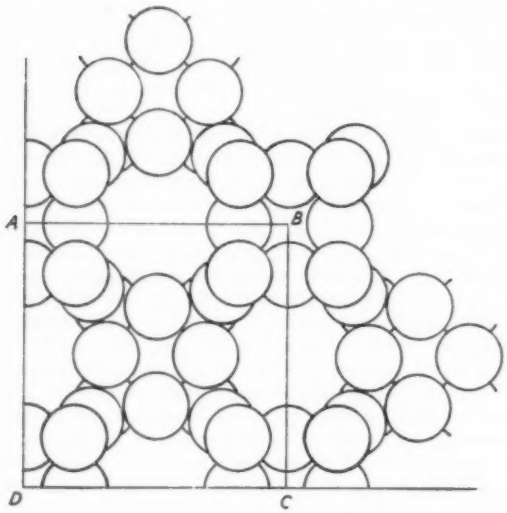

FIG. 3. *The oxygen-atom framework of the structure of* Na-P1. *Oxygen atoms above the plane ABCD are not shown, but a number of those below this plane are indicated.*

Structure. It is possible to build a cubic structure of space group $Im3m$ with 16 (Al + Si) and 32 oxygen atoms per unit cell of size $a = 10{\cdot}0$ Å. Eight $(SiO_4)^{4-}$ tetrahedra are linked in four-membered rings forming a cube-shaped building unit, which is positioned at the corner and body centre of each unit cell. Each unit is linked to its eight nearest neighbours by shared

TABLE 1. *Variation in composition and symmetry of species P.*

	Composition (%) Oxide ratio			Unit cell		
					Contents *	
Sample	Al_2O_3	SiO_2	H_2O	Symmetry	Na	H_2O
1	23·0	45·4	17·6	—	6·0	12·9
	1	3·35	4·30			
2 †	21·8	47·3	17·0	Tetragonal	5·6	12·2
	1	3·68	4·35			
3	21·4	46·6	17·8	Cubic	5·6	13·9
	1	3·70	4·95			
4	21·0	49·2	17·3	Cubic	5·3	12·5
	1	3·98	4·66			
5	19·8	50·4	16·8	Tetragonal	5·1	12·0
	1	4·32	4·75			
6	17·4	53·8	17·5	Cubic	4·4	12·6
	1	5·26	5·72			

* In each case Al + Si = 16.
† Prepared from species Na-*Q* by treatment with N-sodium hydroxide.[3]

oxygen atoms, the resultant framework being shown in Fig. 3. The positions of the atoms will be as follows: [8] 24(O) at 24-fold (*h*) positions, 0*xx*; 8(O) at 8-fold (*c*) positions, $\frac{1}{4}\frac{1}{4}\frac{1}{4}$; 16 (Al + Si) at 16-fold (*f*) positions, *yyy*.

[7] Bragg, *Z. Krist.*, 1930, **74**, 237.
[8] International Tables for *X*-Ray Crystallography, p. 344.

Assuming the tetrahedra to be of regular shape, we would obtain from the symmetry parameters $x = 0{\cdot}188$ and $y = 0{\cdot}156$ and an (Al,Si)–O bond length of 1·65 Å, compared with a bond length of 1·66 Å for an aluminosilicate of this composition.[9] The Si–O–Si bond angles within each building unit are 146° but those linking neighbouring units are 180°. Previously-determined silicate structures lead one to expect Si–O–Si angles not greater than 150°. It seems probable then that the oxygen atoms in the eightfold positions are displaced randomly about the triad axes. This problem, in fact, is similar to that met with in β-cristobalite where the oxygen atoms are displaced from the points required by the observed symmetry elements to give Si–O bonds of 1·63 Å and Si–O–Si angles of 146° and not 180°.[10] The oxygen bridges in Species Na-*P* would have to be shifted 0·43 Å from the triad axis to give a bond angle of 150° and length of 1·65 Å.

Channels. The framework resulting from such an assembly of structural polyhedra has continuous intersecting channels running parallel to the [100] axes (Fig. 3). Each unit cell has a " cage " or " cavity " centred on the cube faces, each of these cages being shared by two

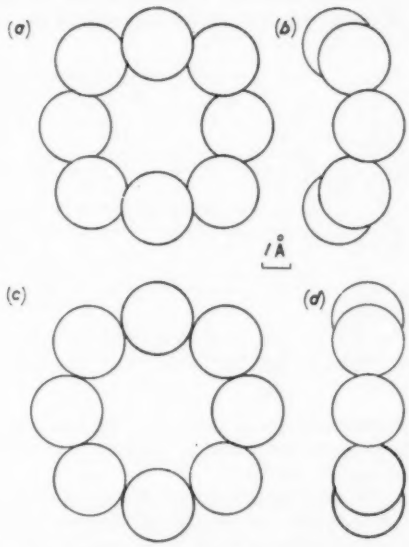

FIG. 4. *(a) and (b): Projections of the 8-membered rings in species* Na-*P in plane and elevation. (c) and (d): Projections of the 8-membered rings in* Na-*Q* [2] *(Linde Sieve A* [3]*), both on the* (100) *plane.*

unit cells and another cage centred on the cube edge, these being shared by four unit cells. Thus there are six complete cages per unit cell, which can be regarded as alternate structural building units made up of two parallel four-membered rings linked to each other *via* four pairs of $(Si,Al)O_4$ tetrahedra, thus forming eight-membered rings which determine the narrowest points in the channel system. These are therefore important factors in determining the size of ions and molecules which might be exchanged or occluded. Fig. 4 is a projection on the (100) plane of one of these eight-membered rings for which the " free " diameter is about 3·2 Å. These rings are non-planar which accounts for their having a much smaller free diameter than the eight-membered rings in species Na-*Q* [2] or Linde Sieve 4A,[1] *i.e.*, 4·2 Å. A projection of the latter ring is also shown in Fig. 4 as are the side views of both types of ring.

Sorption and dehydration on Na-*P* suggest that the minimum " free " diameter must be less than the 3·2 Å which the completely unobstructed rings would give, *i.e.*, the water molecule with a diameter of ~2·76 Å should pass readily through the rings. However, the cationic positions must also be considered in a study of the channel systems.

Cation positions. The maximum number of cations observed per unit cell is 6 (Table 1). It is possible to arrange these in at least three different ways, each fulfilling the cubic symmetry elements. They can be placed at the centres of each of the six cages in the positions $\frac{1}{2}00$, $0\frac{1}{2}0$,

[9] Smith, *Acta Cryst.*, 1954, **7**, 479.
[10] Wells, " Structural Inorganic Chemistry," Cambridge Univ. Press, 1945, pp. 568, 569.

$00\frac{1}{2}$, $0\frac{1}{2}\frac{1}{2}$,$\frac{1}{2}0\frac{1}{2}$, and $\frac{1}{2}\frac{1}{2}0$ (see p. 1528). For Na^+ ions this would leave the channel system with a " free " distance of only ~2·03 Å in certain directions between the cations and the framework, and in other directions a free distance of only ~1·30 Å. A particle diffusing in the channels could however always choose paths which avoid the smaller free distance of ~1·3 Å. Another possible set of positions comprises the six-fold sites $\frac{1}{4}\frac{1}{4}0$, $0\frac{1}{4}\frac{1}{4}$, $\frac{1}{2}0\frac{1}{4}$, $\frac{3}{4}0\frac{1}{2}$, $\frac{1}{2}\frac{3}{4}0$, $0\frac{1}{2}\frac{3}{4}$. These sites are at the centres of half the eight-membered rings, limiting them to " free " diameters of little more than 1·1 Å, *i.e.*, half the channels are effectively blocked. However, if the cations were in a random distribution in a twelve-fold group, *i.e.*, in the positions $\frac{1}{4}0\frac{1}{2}$, $\frac{1}{2}\frac{1}{4}0$, $0\frac{1}{4}\frac{1}{4}$, $\frac{3}{4}\frac{1}{2}0$, $0\frac{3}{4}\frac{1}{2}$, $\frac{1}{2}0\frac{3}{4}$, in addition to those of the second six-fold positions, all the channels would be effectively blocked. In this case the rate of penetration, for example by ammonia and water, might be governed by the mobility of the cations, *i.e.*, the frequency with which they moved from occupied to vacant sites.

Tetragonal and orthorhombic phases. Of the forms of species Na-*P* other than the cubic, the tetragonal cell, with $a = 10{\cdot}0_1$ Å, $c = 9{\cdot}8_3$ Å, would result from a slight distortion of the lattice, the unit cell corners of the cubic and tetragonal forms being in approximately similar positions. The unit cell corners are thus still at the centres of the cubic structural polyhedra. An ideal

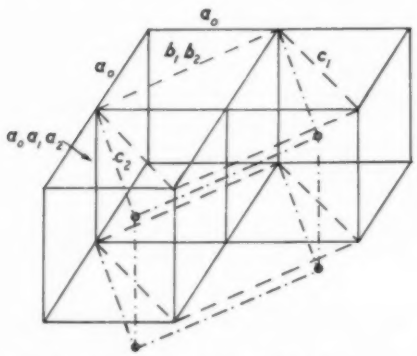

FIG. 5. *Relationship between cubic, orthorhombic, and monoclinic cells which can be derived according to the structure proposed in the Plate for* Na-*P*.

Cubic cell	a_0
Orthorhombic cell	$a_1 b_1 c_1$
Monoclinic cell	$a_2 b_2 c_2$
Mid-points of cubic cells	○

orthorhombic unit cell would be face-centred, but owing to an additional distortion of the framework the centring symmetry vanishes. This lattice is almost identical with that of natural harmotome.

Relationship between the Natural Zeolites of the Harmotome Group and the Synthetic Species.— The symmetry of natural harmotome and phillipsite is not entirely certain. They have been reported monoclinic by Wyart and his co-workers [11,12] but one report [13] and also *X*-ray photographs taken in this laboratory support the idea of a B-face-centred orthorhombic structure for both these minerals, with $a = 9{\cdot}78$, $b = 14{\cdot}00$, $c = 14{\cdot}23$ Å and $a = 9{\cdot}84$, $b = 13{\cdot}85$, $c = 14{\cdot}3$ Å, respectively.

Dimensions of monoclinic unit cells for harmotome [11] and phillipsite [12] are presented in Table 2. Also a monoclinic unit cell (Table 2) can be delineated from the cubic cell of Ba-*P*1

TABLE 2. *Monoclinic cells of harmotome and phillipsite, and the monoclinic cell as calculated from the cubic cell of species P.*

	a (Å)	*b* (Å)	*c* (Å)	β	Cell volume (Å³)
Harmotome	10·00	14·25	8·62	54° 20′	998
Phillipsite	9·80	14·10	8·66	55° 10′	981
From cubic form of Na-*P*	10·01	14·15	8·67	54° 44′	1003

in the manner shown in Fig. 5. All three are practically identical, and contain the same number of framework atoms (Al, Si, and O) per unit cell, but they differ somewhat in composition. Harmotome, which is rich in barium, is siliceous, with an $Al_2O_3 : SiO_2$ ratio of 1 : 4·66 to 1 : 5·15; [13] whereas phillipsite is rich in calcium and has an $Al_2O_3 : SiO_2$ ratio of 1 : 2·57 to

[11] Sekanina and Wyart, *Bull. Soc. franç. Min.*, 1937, **60**, 139.
[12] Wyart and Chatelain, *Bull. Soc. franç. Min.*, 1938, **61**, 121.
[13] Kalb and Klotsch, *Z. Krist.*, 1944, **105**, 315.

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1 : 3·84 with one exceptional ratio reported as 1 : 4·82.[12] The *X*-ray powder patterns of these two minerals are very similar, while those of the sodium-exchanged forms, made by repeated treatments with saturated solutions of sodium chloride until no calcium or barium could be detected in the mother liquor, are almost identical and are close to a barium-exchanged form of Na-*P*2 (Table 3 and Plate). Phillipsite, harmotome and Na-*P* clearly must have similar

TABLE 3. *X-Ray powder patterns.*

	Garronite Tetragonal $a = 10{\cdot}0_1$ Å, $c = 9{\cdot}8_7$ Å		Ion-exchanged derivatives Tetragonal form of Species Na-*P*				Na-exchanged natural harmotome			Garronite Tetragonal $a = 10{\cdot}0_1$ Å, $c = 9{\cdot}8_7$ Å			Ion-exchanged derivatives Tetragonal form of Species Na-*P*				Na-exchanged natural harmotome	
			Ca		Ba								Ca		Ba			
hkl	Int.	*d*	Int.	*d*	Int.	*d*	Int.	*d*		*hkl*	Int.	*d*	Int.	*d*	Int.	*d*	Int.	*d*
110	ms	7·15	s	7·1	m	8·2	m	8·2		204	w	2·22	w	2·20	w	3·24	m	3·25
002	ms	4·95	s	4·94	m	7·2	ms	7·1		323	vw	2·12	w	2·12			m	3·23
211	s	4·12	s	4·12	mw	6·4	m	6·3		422	vw	2·05	mw	2·06	s	3·12	s.diff	3·16
112	m	4·07	ms	4·05			m	5·3										3·15
310	m	3·22	m	3·22	m	4·95	m	5·0		224	vvw	2·03	w	2·02				
103	s	3·14	s	3·12	m	4·28	w	4·28		005	w	1·970	mw	1·975			vw	3·11
222	w	2·88	m	2·87	s	4·14				314	w	1·938	mw	1·930			w	3·08
321	vw	2·68			m	4·05	s	4·08		215	w	1·805	mw	1·805			mw	2·94
213	s	2·66	s	2·66	w	3·88	w	3·90		440	mw	1·770	mw	1·770	vw	2·90	vw	2·91
400	vw	2·54	mw	2·55			w	3·65		522	vw	1·745	mw	1·735			w	2·82
303	w	2·34	m	2·33			w	3·45		414	vw	1·730			w	2·73	m.diff	2·73
																		2·71
										433	mw	1·705	mw	1·705				
										600	vw	1·665	w	1·665	s	2·66	m.diff	2·67
																		2·65
										610	mw	1·645	mw	1·640	w	2·64		
										116	mw	1·605	w	1·605	w	2·57	w	2·54

aluminosilicate frameworks. The vector relationship, derived from Fig. 5, between the monoclinic, orthorhombic B, and cubic minerals is indicated below, where the suffixes 2, 1, and 0 refer respectively to these lattices:

$$a_2 = a_1 \qquad b_2 = b_1 \qquad c_2 = \tfrac{1}{2}(a_1 + c_1)$$

$$a_1 = a_0 \qquad b_1 = b_0 - c_0 \qquad c_1 = b_0 + c_0$$

$$a_2 = a_0 \qquad b_2 = b_0 - c_0 \qquad c_2 = \tfrac{1}{2}(a_0 + b_0 + c_0)$$

X-*Ray Justification for the Structure of* Na-*P*1 (*Cubic*).—Observed intensities for Na-*P*1 were measured photometrically from patterns taken on a Guinier camera, where preferential absorption is minimised by the obliqueness of the incident beam to the slab of powder. Due allowance was made for the absorption by the emulsion of the *X*-ray film.

Theoretical intensities have been calculated for several slightly modified atomic arrangements, based on the structure given on p. 1523, of which only those giving best agreement with the observed intensities are mentioned (Table 4). First, F_c^2m values were calculated for the

TABLE 4. *Observed and calculated relative X-ray intensities for the cubic species of harmotome. The results with * and without † Na^+ cations are given.*

hkl	F_o^2m	F_c^2m *	F_c^2m †	*hkl*	F_o^2m	F_c^2m *	F_c^2m †	*hkl*	F_o^2m	F_c^2m *	F_c^2m †
110	60	51	20	321	300	140	53	510, 431	105	66	22
200	40	53	8	400	16	11	33	521	0	1	11
211	35	1	9	411, 330	19	100	85	440	207	207	247
220	0	10	3	420	0	1	40	530, 433	200	227	227
310	645	493	445	332	0	62	24	600, 442	215	227	215
222	0	35	2	422	44	4	50				

aluminosilicate framework of p. 1523 and compared with observed F_o^2m values ($F_o^2m = I_o/lp$ where m, l, and p denote multiplicity and Lorentz and polarisation factors respectively). This gave fair agreement which was improved both by allowing for a displacement of 8 oxygen atoms away from the triad axis, and by addition of water molecules at the 12-fold [[$\frac{1}{24}$10]]

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positions. At this stage, without inclusion of Na^+ ions, a reliability factor of $R = \sum|F_o^2m - F_c^2m|/\sum F_o^2m$ gave a value of 0·36, when 17 rings were taken into account. Placing the 6 Na^+ ions at $[[\frac{1}{2}00]]$ or nearby worsened the reliability factor to over 0·45.

A Fourier synthesis was also carried out but, on account of the coincidence of diffractions such as 510 and 431 in the powder pattern, only innermost rings could be used. The necessary signs for the observed structure amplitudes were taken from the calculation above and a Fourier projection on the (001) plane, and Fourier sections of the $(100)_0$, $(100)_{\frac{1}{2}}$ and $(110)_0$ planes were evaluated. Individual atoms were not resolved but the general form of the framework was verified, including regions of matter about the 12-fold $[[\frac{1}{2}\frac{1}{2}0]]$ positions. These being assumed to represent the water molecules, no evidence of the six sodium ions could be seen.

Discussion

The structure which has been suggested for the various synthetic phases and natural minerals of the harmotome group of zeolites may be considered in relation to the discontinuity in the dehydration curve obtained for Na-*P*, which is similar to those noted in the dehydration of the fibrous zeolites, scolecite, and natrolite.[14] In addition, Na-*P* gives a differential thermal analysis curve with a very sharp peak [15] of a type found also with the fibrous zeolites.[16] From Fig. 1 it is seen that the step occurs when two molecules of water have been removed per unit cell, and the height of the step corresponds to the removal of another four molecules. Loss of remaining water, nearly half the total, follows a smooth dehydration curve. Each cavity in the structure probably contains one univalent cation and two water molecules, and the step has occurred by the time about half this water has been evolved. Partial dehydration is accompanied by a substantial contraction of the unit cell ($\sim 5\frac{1}{2}\%$).

The contraction, and the similarities to the fibrous zeolites, can be explained as follows. In the harmotome structure as in the fibrous zeolites one can recognise secondary building units in the form of tightly bonded clusters of $(Al,Si)O_4$ tetrahedra (*e.g.*, the cubic anionic units shown in Fig. 3). These are joined by single oxygen bridges to other like units in the harmotome minerals, so that the structure can suffer distortion and shrinkage by diminution in bond angle of these Si–O–(Si,Al) bonds. Only in the fully hydrated form is the structure nearly completely distended. A rather similar situation occurs in the fibrous zeolites. Although tightly bonded clusters of tetrahedra are rather rigidly linked in the direction of the fibre axis, they are more weakly linked by single bonds in the two directions normal to this axis.[17] Hence the unit cell could undergo some shrinkage particularly in these directions during dehydration. Where the lattice alteration is large enough the change is accompanied by a discontinuous discharge of zeolitic water and a step in the dehydration isobar.

In contrast to the situation described above in robust three-dimensional network zeolites such as the chabazite–gmelinite family, the faujasite group, or Linde Sieve A, all the structural polyhedra are not only tightly linked clusters of tetrahedra but they are also linked to other polyhedra by multiple oxygen bridges, leading to frameworks which show minimal lattice changes during dehydration.

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Imperial College, London, S.W.7. [*Received, November 6th*, 1958.]

[14] Milligan and Weiser, *J. Phys. Chem.*, 1937, **41**, 1029.
[15] Barrer and Langley, unpublished work.
[16] Koizumi, *Min. J.* (*Min. Soc., Japan*), 1953, **1**, 36.
[17] Taylor, Meek, and Jackson, *Z. Krist.*, 1933, **84**, 373.

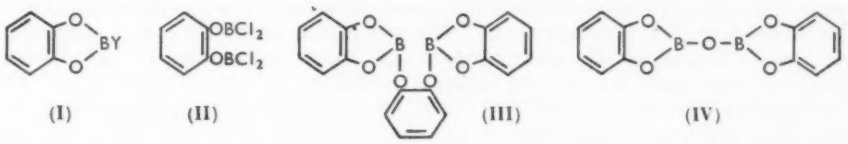
295. *Interaction of Boron Trichloride with Catechol, Quinol, Resorcinol, and Pyrogallol.*

By W. Gerrard, M. F. Lappert, and B. A. Mountfield.

Catechol and boron trihalides readily gave *o*-phenylene halogenoboronates (I; Y = Cl, Br) and tris-*o*-phenylene bisborate (III). From the chloroboronate various derivatives (I; Y = OR, OPh, NR_2, SR, OH) and (IV) were prepared, whilst from catechol two others (I; Y = Ph, Bu^t) were obtained. The chemical properties of these cyclic boron compounds are described. Reactions between resorcinol, quinol, or pyrogallol and boron trichloride gave polymers of variable composition.

In the search for "boron polymers" [1] of satisfactory thermal and hydrolytic stability, reactions of di- and poly-hydric phenols have been examined. With catechol, owing to the proximity of the hydroxyl groups, cyclic boron compounds were formed, whereas with resorcinol, quinol, and pyrogallol the polymers obtained, although satisfactory thermally, were easily hydrolysed, as were all the boron compounds derived from catechol.

Catechol readily gave *o*-phenylene chloroboronate (I; Y = Cl) with one or more mol. of boron trichloride, thus showing that there is a low probability of forming the bis-dichloroborinate (II). The bromoboronate (I; Y = Br) was similarly prepared from boron tribromide. With catechol and boron trichloride in the ratio 3 : 2, the bisborate (III) was readily formed; it was also obtained from catechol and the chloroboronate.



(I) (II) (III) (IV)

The chloroboronate (I; Y = Cl) had exceptional thermal stability, thus resembling ethylene chloroboronate, $(CH_2O)_2B{\cdot}Cl$,[2] but differing from the phenyl analogue, $(PhO)_2B{\cdot}Cl$.[3] Prolonged heating at 220—230° was required in order to demonstrate a clear redistribution into boron trichloride and the bisborate (III). The bromoboronate (I; Y = Br) had comparable stability and this is of interest because earlier [4] attempts to prepare bromoboronates $(RO_2)B{\cdot}Br$ and dibromoborinates $RO{\cdot}BBr_2$ have failed, although one bromoborinate $Ph{\cdot}B(OBu^n)Br$ is known.[5]

Both the *o*-phenylene halogenoboronates reacted with alcohols or phenol to give borates (I; Y = OR or OPh). With a controlled amount of water, the chloroboronate afforded *o*-phenylene hydrogen borate (I; Y = OH). Thiols reacted slowly with the chloroboronate, but prolonged heating gave the thio-esters (I; Y = SBu^n and $S{\cdot}C_8H_{17}$-*n*). Both the halogenoboronates formed stable 1 : 1 complexes with pyridine. With a secondary amine (2 mol.) the chloroboronate (1 mol.) gave an *o*-phenylene dialkylaminoboronate (I; Y = NEt_2 and NBu^n_2) and dialkylammonium chloride; these dialkylaminoboronates were appreciably more stable than the di-*n*-butyl dialkylaminoboronates,[6] the only other known compounds of this class.

o-Phenylene hydrogen borate (I; Y = OH) is an example of the very rare partially hydrolysed esters [2] of boric acid. When heated it afforded the anhydride (IV), which was

[1] Gerrard, *Chem. Prod.*, 1957, **20**, 489.
[2] Blau, Gerrard, and Lappert, *J.*, 1957, 4116.
[3] Colclough, Gerrard, and Lappert, *J.*, 1955, 907.
[4] Bujwid, Gerrard, and Lappert, *Chem. and Ind.*, 1957, 1386; Goubeau, Becher, and Griffel, *Z. anorg. Chem.*, 1956, **282**, 86.
[5] Abel, Gerrard, and Lappert, *J.*, 1957, 5051.
[6] Gerrard, Lappert, and Pearce, *Chem. and Ind.*, 1958, 292.

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converted into the halogenoboronate with boron trihalide (Cl,Br) and into the chloroboronate with phosphorus pentachloride. With alcohols, the anhydride was converted into the esters (I; Y = OR). The anhydride was also prepared from catechol and boric acid by azeotropic removal of water by use of benzene.

Pyrolysis of methyl *o*-phenylene borate (I; Y = OMe) gave trimethyl borate and the bisborate (III), whereas other *n*-alkyl esters were stable; the *sec.*-butyl ester, however, was almost completely decomposed into but-2-ene and the anhydride (pyroborate; IV).

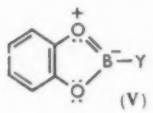
Boron trichloride and the *n*-butyl ester (I; Y = OBu^n) readily gave *o*-phenylene chloroboronate and *n*-butyl dichloroborinate, $Bu^nO{\cdot}BCl_2$.[7] The bromoboronate, together with methyl bromide, was similarly obtained from methyl *o*-phenylene borate and boron tribromide. Alkyl, as well as phenyl, *o*-phenylene borates formed stable 1 : 1-complexes with pyridine; this is of interest because trialkyl borates do not as a rule form amine complexes, whereas triaryl borates do owing to decreased back-co-ordination, .[3,8] The alkyl *o*-phenylene borates may be regarded as mixed alkyl aryl borates, and evidently the boron atom in them is sufficiently electrophilic to permit co-ordination to take place.

n-Butyl *o*-phenylene borate was also prepared from catechol and either tri-*n*-butyl borate or butan-1-ol and boric acid.

The *S*-alkyl *o*-phenylene thioborates (I; Y = SR) were readily hydrolysed by cold water affording the thiol, catechol, and boric acid. Butan-1-ol was not displaced by octanethiol by heating *n*-butyl *o*-phenylene borate with octanethiol, but the *n*-butylthio-group in *S*-*n*-butyl *o*-phenylene thioborate was replaced by the *n*-octyloxy-group by reaction with octanol. A substituted amino-group attached to a boron atom is replaceable by an alkoxy-group but not the reverse;[9] it is now evident that a thiol group attached to boron is replaceable by an alkoxy-group, and again not conversely. The *S*-alkyl *o*-phenylene thioborates are the first reported examples of monothio-boric esters.

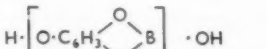
o-Phenylene phenylboronate[10,11] (I; Y = Ph) was obtained by azeotropic removal of water from a mixture of phenylboronic anhydride $(PhBO)_3$ and catechol, and *o*-phenylene *tert.*-butylboronate (I; Y = Bu^t) was prepared by treating *tert.*-butylboron dichloride with catechol.

Compounds of type (I) possess considerable thermal stability and this is greater than in corresponding acyclic compounds of type $(RO)_2B{\cdot}Y$. This may be attributed to stabilisation by cyclisation (cf. ref. 2), but may in part also be due to the fact that the boron-containing ring can exhibit 6π-electron resonance, giving rise to canonical structures of the type (V). Evidence for this view has recently been obtained from ultraviolet spectra of *o*-phenylene phenylboronate.[11]



(V)

(VI)



(VII)

With resorcinol, quinol, and pyrogallol no volatile materials or bisdichloroborinates were obtained. With an excess of boron trichloride, resorcinol afforded a trinuclear compound $[Cl_2B{\cdot}O{\cdot}C_6H_4{\cdot}O{\cdot}B(Cl){\cdot}O]_2C_6H_4$. All other products were polymeric and appeared to correspond to (VI) for the dihydric phenols and to (VII) for pyrogallol. The chlorine-containing polymers lost boron trichloride when heated, presumably forming polymeric

[7] Gerrard and Lappert, *J.*, 1951, 2545; 1955, 3084.
[8] Colclough, Gerrard, and Lappert, *J.*, 1956, 3006; Abel, Gerrard, Lappert, and Shafferman, *J.*, 1958, 2895.
[9] Gerrard, Lappert, and Pearce, *J.*, 1957, 381.
[10] Kuivila, Keough, and Soboczenski, *J. Org. Chem.*, 1954, **19**, 780.
[11] Dewar, Kubba, and Pettit, *J.*, 1958, 3076.

cross-linked borates. Hydrolysis of all products invariably afforded the parent polyhydric phenol and boric acid. The polymers were generally insoluble in non-polar solvents.

Experimental.

o-Phenylene Halogenoboronates.—Catechol (3·76 g., 1 mol.) was added in suspension in methylene chloride to boron trichloride (4·67 g., 1·17 mol.) at −80°. As the system warmed to 15°, hydrogen chloride (2·27 g., 91%) and boron trichloride (0·66 g.) were absorbed by potassium hydroxide, and the residue (5·1 g., after being kept at 20°/15 mm.) gave *o-phenylene chloroboronate* (4·88 g., 92%), b. p. 64°/10 mm., m. p. 57° (Found: C, 47·0; H, 2·5; Cl, 22·4; B, 6·9; $C_6H_4O_2$, 69·4. $C_6H_4O_2ClB$ requires C, 46·7; H, 2·6; Cl, 23·0; B, 7·0; $C_6H_4O_2$, 70·0%). Similarly *o-phenylene bromoboronate* (6·24 g., 90%), b. p. 76°/9 mm., m. p. 47° (Found: Br, 39·9; B, 5·4. $C_6H_4O_2BrB$ requires Br, 40·2; B, 5·4%), and hydrogen bromide (5·45 g., 97%) were obtained from boron tribromide and catechol.

The chloroboronate (3·25 g.) was recovered in 96·4% yield after it had been heated at 55—60°/15 mm. for 12 hr., the remaining material being accounted for as boron trichloride (0·035 g.) and an undistilled residue (Found: B, 6·5%). Similarly the bromoboronate was recovered in 75·6% yield, the remainder having given boron tribromide and a residue (Found: B, 6·5%). At 220—230° (23·25 hr.), the chloroboronate (8·4 g.) gave boron trichloride (0·28 g.), and tris-*o*-phenylene bisborate (1·03 g.), b. p. 180°/0·02 mm., m. p. 102° (Found: B, 6·2; Cl, 0. Calc. for $C_{18}H_{12}O_6B_2$: B, 6·26; Cl, 0%); and was partly recovered (6·4 g., 76%), b. p. 57°/5 mm. (Found: Cl, 22·4; B, 7·0%).

The chloroboronate (7·4 g., 1 mol.) was shaken with a suspension of water (2·6 g., 3 mol.) in ether (40 c.c.), and immediately at 20°/15 mm. hydrogen chloride (1·74 g., 99%) was evolved. The solid residue (8·2 g.) was separated by benzene into boric acid (2·9 g., 98%) and catechol (5·1 g., 97%), b. p. 120°/10 mm., m. p. 103—104°. Hydrogen bromide (0·85 g., 95%), boric acid (0·69 g., 100%), and catechol (1·22 g., 100%), m. p. and mixed m. p. 103—104°, were similarly obtained from the bromoboronate (2·21 g.).

When only 1 mol. of water was used with the chloroboronate (7·6 g., 1 mol.), there was no precipitation from the ether. On removal of solvent, hydrogen chloride (1·77 g., 99%) was evolved, and the residue of *o-phenylene hydrogen borate* (6·7 g., 100%), m. p. 70—75° (Found: C, 52·4; H, 3·7; B, 8·0. $C_6H_5O_3B$ requires C, 52·9; H, 3·7; B, 8·0%), afforded water (in 80% yield) and *di-o-phenylene pyroborate* (96%) (see also ref. 13), b. p. 160°/0·1 mm. (Found: C, 56·0; H, 3·2; B, 8·5. $C_{12}H_8O_5B_2$ requires C, 56·8; H, 3·2; B, 8·5%). Acidic hydrogen was absent. This anhydride (45·4 g., 89%), b. p. 160°/0·1 mm. (Found: B, 8·3; $C_6H_4O_2$, 84·9. Calc. for $C_{12}H_8O_5B_2$: B, 8·5; $C_6H_4O_2$, 85·2%), together with an undistilled residue (2·8 g.) (Found: B, 7·2%), was also obtained by the azeotropic (benzene, 50 c.c.) removal of water from a mixture of catechol (44·0 g., 1 mol.) and boric acid (24·7 g., 1 mol.).

Di-o-phenylene Pyroborate.—The pyroborate (3·4 g., 1 mol.) shaken with water (1·2 g., 5 mol.) in benzene (25 c.c.) immediately afforded boric acid (1·66 g., 100%), isolated by filtration, and catechol (2·8 g., 95%), m. p. 102—103°, obtained from the filtrate by removal of solvent at 20°/0·1 mm. After being heated for 12 hr. at 290°, the pyroborate (Found: B, 8·6%) was recovered in 89% yield, and there was a black residue. Boron trifluoride in methylene chloride was without determined action, the anhydride (Found: B, 8·4%) being recovered in 91% yield, whereas the anhydride (5·63 g., 1 mol.) and boron trichloride (3·37 g., 1·3 mol.) in methylene chloride (10 c.c.) gave at 20° (48 hr.) boron trichloride (1·57 g.), removed at 20°/15 mm., *o*-phenylene chloroboronate (5·4 g., 79%), b. p. 67°/10 mm., m. p. 56° (Found: Cl, 22·5; B, 7·1%), the anhydride (0·92 g.), and a residue (0·75 g.) (Found: B, 2·6%). Corresponding results with the anhydride (6·06 g., 1 mol.) and boron tribromide (6·0 g., 1 mol.) were: tribromide recovery (1·55 g.), *o*-phenylene bromoboronate (6·5 g., 68%), b. p. 78°/10 mm., m. p. 48° (Found: Br, 40·1; B, 5·4%), anhydride recovery (1·2 g.), and a residue (1·1 g.) (Found: B, 16·0%).

Phosphorus pentachloride (6·6 g.) was heated with the anhydride (6·7 g.) at 120—140° for 4 hr. A liquid trapped at −80° contained boron trichloride (0·9 g.) (pyridine complex, m. p. 110° [14]). The residue gave phosphorus oxychloride (2·8 g., 69%), b. p. 106—108° (Found:

[12] Thomas, *J.*, 1946, 820, 823.
[13] Schäfer and Braun, *Naturwiss.*, 1952, **39**, 280.
[14] Gerrard and Lappert, *J.*, 1951, 1020.

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Cl, 68·4. Calc. for $POCl_3$: Cl, 69·4%), *o*-phenylene chloroboronate (4·9 g., 60%), b. p. 66°/10 mm., m. p. 57° (Found: Cl, 22·7; B, 6·9%), and a non-volatile residue (1·2 g.).

Alkyl o-Phenylene Borates.—Butan-1-ol (4·2 g., 1 mol.) in methylene chloride (5 c.c.) was added to *o*-phenylene chloroboronate (8·6 g., 1 mol.) in methylene chloride (15 c.c.) at 15°. Hydrogen chloride (1·84 g., 91%) was evolved, and n-*butyl o-phenylene borate* (9·5 g., 89%), b. p. 106°/5 mm., n_D^{20} 1·4891, d_4^{20} 1·0707, $[R_L]_D$ 51·74 (Calc. 51·62) (Found: C, 62·4; H, 7·1; B, 5·7; $C_6H_4O_2$, 55·6. $C_{10}H_{13}O_3B$ requires C, 62·5; H, 6·8; B, 5·6; $C_6H_4O_2$, 56·3%), and a residue (1·0 g.) (Found: B, 6·2%) were obtained. Similarly other esters were prepared; the essential details are shown in the Table. Hydrogen chloride determined varied from 91 to 97%.

Phenyl *o*-phenylene borate, m. p. 44° (Found: C, 67·2; H, 4·4; B, 5·2. Calc. for $C_{12}H_9O_3B$: C, 68·0; H, 4·3; B, 5·1%), previously prepared [12] by the azeotropic technique, was similarly obtained.

The *n*-butyl ester (45·2 g., 86%), b. p. 106°/6 mm. (Found: B, 5·6%), was also prepared by heating catechol (30 g., 1 mol.) with tri-*n*-butyl borate (62·8 g., 1 mol.) under a Vigreux column, butan-1-ol (38·2 g., 97%) being distilled off; the ester was prepared (85% yield) from *o*-phenylene bromoboronate and butan-1-ol, hydrogen bromide (95%) being collected. A fourth method of preparing the *n*-butyl ester (33·2 g., 86%), b. p. 106°/5 mm. (Found: B, 5·6%), comprised the azeotropic separation of water (10·9 c.c., 100%) from a mixture of catechol (22·0 g., 1 mol.), boric acid (12·4 g., 1 mol.), and butan-1-ol in excess. There was an undistilled residue (2·0 g.) (Found: B, 6·3%).

The *sec.*-butyl ester (9·4 g., 69%), b. p. 97°/5 mm. (Found: B, 5·6%), was also obtained by heating (2 hr.) a mixture of *o*-phenylene pyroborate (9·0 g.) and the alcohol (20 c.c. excess) under reflux, followed by distillation.

Alkyl o-phenylene borates.

Ester	Yield (%)	Found (%) / Calc. (%) C	H	B	B. p. (°/mm.)	n_D^{20}	d_4^{20}	Molar refractivity Found	Calc.†
Me	82	56·2	4·8	7·2	81°/10	1·5059	1·1890	37·45	37·68
		56·1	4·7	7·2					
Et	89	58·1	5·8	6·6	91/10	1·4960	1·1316	42·30	42·33
		58·6	5·5	6·6					
Pr^n	91	60·8	6·4	6·1	105/10	1·4900	1·0937	47·03	46·98
		60·7	6·2	6·1					
Bu^n	88	62·4	7·1	5·7	104/5	1·4891	1·0707	51·74	51·62
		62·5	6·8	5·6					
Bu^i	77	62·5	6·7	5·6	100/5	1·4846	1·0558	52·08	51·62
Bu^s	88	62·9	7·1	5·7	97/5	1·4853	1·0704	51·43	51·62
n-C_5H_{11}	94	65·1 *	7·4	5·2	116/5	1·4891	1·0578	56·22	56·27
		64·1	7·3	5·3					
n-C_8H_{17}	92	67·7	8·4	4·4	124/0·05	1·4856	1·0158	70·09	70·21
		67·7	8·5	4·4					

* Repeated.

† Calculations based on Vogel's values (*J.*, 1943, 638; 1946, 133; 1948, 616, 654), the value 2·28 being assigned to boron.

After methyl *o*-phenylene borate (5·2 g.) had been heated at 240° for 16·5 hr., trimethyl borate (1·1 g., 92%), b. p. 68° (Found: B, 10·4. Calc. for $C_3H_9O_3B$: B, 10·4%), and tri-*o*-phenylene bisborate (3·4 g., 85%), b. p. 168°/0·01 mm., m. p. 100—102° (Found: B, 6·3%), were obtained. Octyl *o*-phenylene borate (6·2 g.), however, was recovered (5·7 g.), b. p. 115°/0·01 mm. (Found: B, 4·4%), after being refluxed at 350° for 12 hr.

Similarly the *n*-butyl ester (7·9 g.) was recovered in 96% yield (Found: B, 5·6%) after being heated at 280° for 24 hr. The *sec.*-butyl ester (6·9 g.), however, at 330° (12 hr.) gave but-2-ene (1·81 g., 90%) (2 : 3-dibromobutane, b. p. 157°, $n_D^{20\cdot5}$ 1·5109), and *o*-phenylene pyroborate (4·2 g., 92%), b. p. 155°/0·05 mm. (Found: B, 8·4%).

Addition of the butyl ester (8·0 g., 1 mol.) to boron trichloride (4·9 g., 1 mol.) at −80°, followed by warming to 15°, gave at 20°/0·1 mm. *n*-butyl dichloroborinate (6·2 g., 96%), b. p. 39—43°/18—20 mm. (Found: Cl, 45·9; B, 7·0. Calc. for $C_4H_9OCl_2B$: Cl, 45·8; B, 7·0%) (first collected at −80°), and a residue of *o*-phenylene chloroboronate (6·1 g., 95%), m. p. 54° (Found: Cl, 22·0; B, 7·1%).

The methyl ester (6·6 g., 1 mol.) added to boron tribromide (11·0 g., 1 mol.) at 15° afforded at 60° methyl bromide (3·8 g., 91%) (Found: Br, 85·0. Calc. for CH_3Br: Br, 84·2%) (collected at −80°), followed at 60°/20 mm. by boron tribromide (3·1 g., 85%), b. p. 91°, pyridine complex, m. p. 125° (Found: Br, 71·0; B, 3·3; C_5H_5N, 24·2. Calc. for $C_5H_5NBr_3B$: Br, 72·7; B, 3·3; C_5H_5N, 24·0%), and at higher temperature by *o*-phenylene bromoboronate (7·0 g., 80%), b. p. 79°/10 mm., m. p. 47° (Found: Br, 39·8; B, 5·5%), leaving a residue (2·0 g.) (Found: Br, 14·8; B, 14·6%).

The *n*-butyl ester (4·6 g., 1 mol.) was shaken with water (1·3 g., 3 mol.) and benzene (30 c.c.). Boric acid (1·46 g., 99%) was immediately formed and filtered off, and catechol (2·4 g., 91%) was obtained from the filtrate.

Similarly, the octyl ester (7·6 g., 1 mol.) gave boric acid (1·84 g., 97%); catechol (2·9 g., 86%), m. p. and mixed m. p. 105°, was obtained by evaporation of the solvent and addition of *n*-pentane.

Tri-o-phenylene Bisborate.—Whereas catechol (3·2 g., 1 mol.) suspended in methylene chloride (15 c.c.) and boron trichloride (6·8 g., 2 mol.) afforded boron trichloride (3·14 g., 0·92 mol.) and *o*-phenylene chloroboronate (4·2 g., 93%), b. p. 62°/10 mm., m. p. 57° (Found: Cl, 22·6; B, 7·2%), instead of the bisdichloroborinate, the use of 3 mol. of catechol (7·4 g.) and 2 mol. of boron trichloride (5·2 g.), mixed at −80° and allowed to warm to 20°, afforded hydrogen chloride (4·8 g., 98%) and tri-*o*-phenylene bisborate (7·6 g., 98%), b. p. 170—175°/0·03 mm. (Found: B, 6·3%). Similarly, from 3 mol. of catechol (9·6 g.) and 1 mol. of boron trichloride (3·4 g.), catechol (3·7 g.), b. p. 120°/10 mm., m. p. 101—104°, and the bisborate (4·0 g.), b. p. 175—180°/0·03 mm., m. p. 104° (Found: B, 6·1%), were obtained. The bisborate (3·1 g., 95%), b. p. 175—180°/0·03 mm., m. p. 105° (Found: C, 62·5; H, 4·9; B, 6·2. Calc. for $C_{18}H_{12}O_6B_2$: C, 62·5; H, 3·5; B, 6·3%), was obtained from the chloroboronate (2·9 g., 2 mol.) and catechol (1·0 g., 1 mol.), mixed in methylene chloride (10 c.c.) at −80°, and warmed to 20°

On being shaken with water (0·6 g., 6 mol.), the bisborate (1·9 g., 1 mol.) in benzene (25 c.c. immediately gave a precipitate of boric acid (0·68 g., 100%), and catechol (1·8 g., 99%), m. p. 102—104°, was obtained from the solvent.

After the bisborate (3·8 g.) had been heated at 290° for 12 hr., 82% was recovered, b. p. 175—180°/0·03 mm., m. p. 104° (Found: B, 6·2%), there being a black residue (0·6 g.).

Pyridine Complexes.—Pyridine–methyl o-*phenylene borate* (7·8 g., 93%), m. p. 161—163°, after being washed with pentane, stable at 20°/0·01 mm. (5 hr.) (Found: B, 4·8; C_5H_5N, 34·6. $C_{12}H_{12}O_3NB$ requires B, 4·7; C_5H_5N, 34·7%), was obtained from the base (2·9 g., 1 mol.) and the borate (5·5 g., 1 mol.) mixed at −80° and warmed to 20°. *Pyridine–ethyl* o-*phenylene borate* (5·7 g., 94%), m. p. 130—140° (Found: B, 4·5; C_5H_5N, 33·0. $C_{13}H_{14}O_3NB$ requires B, 4·45; C_5H_5N, 32·6%), was precipitated on mixing the ester (4·1 g.) and base (1·98 g.) in *n*-pentane. It lost 1·3% of its weight in 5 hr. at 20°/0·005 mm.

Similarly *pyridine–*n-*propyl* o-*phenylene borate* (95%), m. p. 148—151° (Found: B, 4·2; C_5H_5N, 31·0. $C_{14}H_{16}O_3NB$ requires B, 4·2; C_5H_5N, 30·8%), was obtained, but the initial oil had to be heated in the mixture to obtain the solid complex before filtration. This was also necessary for *pyridine–*n-*butyl* o-*phenylene borate* (73%), m. p. 160—165° (Found: B, 4·0; C_5H_5N, 30·2. $C_{15}H_{18}O_3NB$ requires B, 4·0; C_5H_5N, 29·2%), which lost 0·7% of its weight in 5 hr. at 20°/0·001 mm. *Pyridine–phenyl* o-*phenylene borate* (95% yield), m. p. 135—138°, stable at 20°/0·02 mm. (5 hr.) (Found: B, 3·9; C_5H_5N, 26·6. $C_{17}H_{14}O_3NB$ requires B, 3·7; C_5H_5N, 27·2%), was similarly prepared, a mixture of *n*-pentane (5 vol.) and methylene chloride (1 vol.) being used as a medium. In this way, too, *pyridine–o-phenylene chloroboronate* (97% yield), m. p. 80—90°, stable at 20°/0·01 mm. (3 hr.) (Found: B, 4·6; C_5H_5N, 33·8. $C_{11}H_9O_2NClB$ requires B, 4·6; C_5H_5N, 33·9%), and *pyridine* o-*phenylene bromoboronate* (100%), m. p. 80—85°, stable at 20°/0·005 mm. (3 hr.) (Found: B, 3·8; C_5H_5N, 28·4. $C_{11}H_9O_2NBrB$ requires B, 3·9; C_5H_5N, 28·5%), were obtained from the halogenoboronates. The complexes were easily hydrolysed.

S-*Alkyl* o-*Phenylene Thioborates.*—*n*-Butanethiol (6·2 g., 2·2 mol.) and *o*-phenylene chloroboronate (4·8 g., 1 mol.) were heated at 150—160° for 4 hr., and hydrogen chloride (1·07 g., 94%), *n*-butanethiol (3·4 g., excess of 1 mol.), and S-n-*butyl* o-*phenylene thioborate* (5·1 g., 79%), b. p. 80—84°/0·1 mm., n_D^{20} 1·5334 (Found: S, 15·9; B, 5·2. $C_{10}H_{13}O_2SB$ requires S, 15·4; B, 5·2%) were obtained. Evolution of hydrogen chloride was slow at 20° (23·2% after 4·5 hr.), but within ½ hr. at 150—160° a further 58% of gas was liberated.

Similarly, S-*octyl* o-*phenylene thioborate* (11·3 g., 93%), b. p. 142°/0·05 mm., n_D^{20} 1·5198

(Found: C, 64·2; H, 8·0; B, 4·1. $C_{14}H_{21}O_2SB$ requires C, 63·6; H, 8·0; B, 4·1%), was obtained at 200—220°.

With water (1·2 g., 3 mol.) the *n*-butyl thio-ester (4·65 g.) readily afforded *n*-butanethiol (2·0 g., 99%), b. p. 98°, n_D^{20} 1·4420, boric acid (1·3 g., 94%), and catechol (2·25 g., 92%), m. p. 102—103°, mixed m. p. 103°.

No reaction was observed when a mixture of *n*-butyl *o*-phenylene borate (1 mol.) and octanethiol (1 mol.)was heated at 200° for 1 hr., the reagents being recovered upon distillation. Similarly, no reaction was apparent between *n*-butanethiol and ethyl *o*-phenylene borate. By contrast, from octanol (2·60 g., 1 mol.) and *S*-*n*-butyl *o*-phenylene thioborate (4·10 g., 1 mol.), *n*-butanethiol (1·70 g., 96%), b. p. 98°, n_D^{20} 1·4435, and octyl *o*-phenylene borate (4·60 g., 93%), b. p. 126°/0·05 mm., n_D^{20} 1·4854 (Found: B, 4·3%), were obtained.

o-*Phenylene Dialkylaminoboronates*.—Diethylamine (18·0 g., 2 mol.) in *n*-pentane (50 c.c.) was added to *o*-phenylene chloroboronate (19·0 g., 1 mol.) in *n*-pentane (100 c.c.) at −80°. The mixture was warmed to 20° and set aside for 18 hr. The white precipitate of diethylammonium chloride (13·6 g., 100%) (Found: Cl, 31·7. Calc. for $C_4H_{12}NCl$: Cl, 32·3%) was filtered off and washed with *n*-pentane. The filtrate afforded o-*phenylene diethylaminoboronate* (18·6 g., 79%), b. p. 72°/0·1 mm., n_D^{20} 1·5061 (Found: C, 62·5; H, 7·5; N, 7·4; B, 5·6. $C_{10}H_{14}O_2NB$ requires C, 62·9; H, 7·3; N, 7·3; B, 5·7%), and a non-volatile residue (0·50 g.) (Found: B, 4·4%).

Similarly, from di-*n*-butylamine (29·3 g.) and the chloroboronate (17·5 g.) there were obtained di-*n*-butylammonium chloride (18·6 g., 96%) (Found: Cl, 21·5. Calc. for $C_8H_{20}NCl$: Cl, 21·4%) and o-*phenylene di*-n-*butylaminoboronate* (23·0 g., 82%), b. p. 108°/0·005 mm., n_D^{20} 1·4971 (Found: C, 67·6; H, 8·7; N, 5·6; B, 4·4. $C_{14}H_{22}O_2NB$ requires C, 68·1; H, 8·9; N, 5·7; B, 4·4%).

o-*Phenylene Alkyl(and Aryl)boronates*.—A mixture of benzene (30 c.c.), phenylboronic anhydride [15] (6·11 g., 1 mol.), and catechol (6·50 g., 1 mol.) was heated under a Vigreux column fitted with a Dean and Stark head. Water (1·00 g., 94%) was separated from the first fraction, which was the water–benzene azeotrope. The residue (11·55 g.), after removal of benzene, afforded *o*-phenylene phenylboronate (10·73 g., 93%), m. p. 111°, b. p. 124°/0·4 mm. (Found: C, 73·9; H, 4·6. Calc. for $C_{12}H_9O_2B$: C, 73·5; H, 4·6%).

Catechol (4·00 g., 1 mol.) in suspension in methylene dichloride (35 c.c.) was added to *tert*.-butylboron dichloride [16] (5·02 g., 1 mol.) at 20°; the reaction was endothermic and hydrogen chloride was evolved. Matter volatile at 20°/0·5 mm. was removed and the residue (6·07 g.) afforded o-*phenylene* tert.-*butylboronate* (5·89 g., 92%), b. p. 40—41°/0·4 mm., n_D^{20} 1·4924, d_4^{20} 1·016 (Found: C, 67·7; H, 7·4. $C_{10}H_{13}O_2B$ requires C, 68·2; H, 7·45%).

Interaction of Resorcinol and Boron Trichloride.—Resorcinol (2·82 g., 1 mol.) suspended in methylene chloride (50 c.c.) was added to boron trichloride (6·0 g., 2 mol.) at −80°, and after 1 hr. the mixture was warmed to 25°. Boron trichloride (2·06 g., 0·69 mol.) and hydrogen chloride (1·82 g., 1·95 mol.) were removed at 25°/3 mm., leaving the solid $[Cl_2B{\cdot}O{\cdot}C_6H_4{\cdot}O{\cdot}B(Cl){\cdot}O]_2C_6H_4$ (4·81 g., 0·323 mol.) (Found: Cl, 34·6; B, 7·45. Calc. for $C_{18}H_{12}O_6Cl_6B_4$: Cl, 36·6; B, 7·45%). Yields are based on: $C_6H_4(OH)_2 + 2BCl_3 \longrightarrow 2HCl + [C_6H_4(OBCl_2)_2] \longrightarrow \frac{1}{3}[Cl_2B{\cdot}O{\cdot}C_6H_4{\cdot}O{\cdot}B(Cl){\cdot}O]_2C_6H_4 + \frac{2}{3}BCl_3$.

Similarly (6·5 g., 1 mol.) of resorcinol and 1 mol. of the trichloride gave hydrogen chloride (4·3 g., 2 mol.) and a solid at 20°/0·05 mm. (9·35 g.), probably a polymer of type (VI) [Found: Cl, 21·2; B, 6·91%; Cl : B = 1 : 1·06. Calc. for (VI; $n = 9$): Cl, 21·4; B, 6·50%; Cl : B = 1 : 1·00], which was soluble in acetone, but insoluble in ether, chloroform, benzene, and pentane. When this product (5·42 g.) was heated at 300°/0·3 mm. (5 hr.), boron trichloride (0·955 g.) was evolved, leaving a glass (4·17 g.) (Found: Cl, 7·5; B, 5·8%), of which 1·62 g. readily afforded boric acid (0·47 g., 88%) and resorcinol (1·3 g., 91%) when shaken with water (0·47 g., 3 mol. for 1 g. atom of boron) and ether (20 c.c.).

Interaction of Quinol and Boron Trichloride.—Quinol (10·6 g., 3 mol.), suspended in methylene chloride (50 c.c.), was added to boron trichloride (7·6 g., 2 mol.) at −80°, and the mixture was warmed to 20°. At 20°/15 mm. hydrogen chloride (4·3 g., 3·7 mol.) was removed and there was a solid residue (13·5 g.), probably a polymer (VI) [Found: Cl, 18·4; B, 5·2%; Cl : B = 1 : 1·04. Calc. for (VI; $n = 3$): Cl, 18·6; B, 5·6%]. With water (0·53 g.) suspended in ether (10 c.c.), a portion (2·01 g.) immediately gave hydrogen chloride (0·35 g.), boric acid (0·56 g.), and quinol (1·47 g., 94%), m. p. and mixed m. p. 168°.

[15] Bean and Johnson, *J. Amer. Chem. Soc.*, 1932, **54**, 4415.
[16] McCusker, Ashby, and Makowski, *ibid.*, 1957, **79**, 5182.

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Interaction of Pyrogallol and Boron Trichloride.—Pyrogallol (6·3 g., 1 mol.) suspended in methylene chloride (40 c.c.) was added to boron trichloride (5·9 g., 1 mol.) at −80°. The reaction constituents were then separated at 30°/0·07 mm. into hydrogen chloride (5·1 g., 93%) and a white solid (7·2 g.) (Found: B, 7·2%), considerable difficulty being experienced in removing last traces of solvent, accomplished at 100°/0·01 mm. (1 hr.) [Found: B, 8·0%; *M*, ~700 (ebullioscopic in $CHCl_3$). Calc. for (VII; $m = 5$): B, 7·9%; *M*, 698]. This white solid lost 6·5% of its weight at 300°/0·01 mm. (1 hr.) becoming deep red and extremely hard and tough [Found: B, 8·4%; *M*, *ca.* 500 (ebullioscopic in $CHCl_3$)]. Both solids were quantitatively hydrolysed to boric acid on being shaken (1 hr.) with water suspended in ether.

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296. *A Simple Melting-point Calorimeter for Moderately Precise Determinations of Purity.*

By J. H. BROOKS and G. PILCHER.

A melting-point calorimeter has been constructed for a rapid (3—4 hr.) determination of the purity of a 3 ml. sample by measurement of the solid–liquid equilibrium temperature as a function of the fraction which is liquid. The heat of fusion is determined to about ±10% and the molar percentage of impurity to about ±20%. Melting points, heats of fusion, and purities are given for diverse samples of m. p. −140° to −14°.

THE reliability of a measured physical property depends on the purity of the sample. A generally applicable method for determining the purity of an organic sample is to compare its freezing point with the value for zero impurity. Time–temperature analysis of controlled freezing or melting is widely used for this, the most accurate methods being those developed by the American Petroleum Institute Research Project 6.[1] An alternative is the calorimetric procedure in which the solid–liquid equilibrium temperature is measured as a function of the fraction of the sample liquid. The two procedures have been experimentally compared by Glasgow *et al.*[2] In the calorimetric method, the depression of freezing point and the heat of fusion, and thereby the cryoscopic constant, are determined in a single experiment and this procedure can yield more precise results than the former. Low-temperature specific heat calorimeters are used to investigate purity during entropy determinations,[3] but are too complex for this to be their main use. Consequently several calorimeters designed for purity determinations only have been described. Pilcher's [4] is very precise but requires a 50 ml. sample and Aston, Fink, Tooke, and Cines's [5] is rather complex. Tunnicliff and Stone [6] described a moderately precise semi-automatic apparatus. One of the simplest designs, that by Clarke, Johnston, and de Sorbo,[7] requires only 3 ml. but has the disadvantage that the calorimetric conditions are not strictly adiabatic. The calorimeter now described has been developed from that design and determines purities of small samples of a wide variety of compounds comparatively rapidly (3—4 hr.) with moderate precision.

The theory of the calorimetric method has been given by Rossini.[8] For samples in

[1] Mair, Glasgow, and Rossini, *J. Res. Nat. Bur. Stand.*, 1941, **26**, 591; Glasgow, Streiff, and Rossini, *ibid.*, 1945, **35**, 355.
[2] Glasgow, Ross, Horton, Enagonis, Dixon, Saylor, Furukawa, Reilly, and Henning, *Analyt. Chim. Acta*, 1957, **17**, 54.
[3] Ruhrwein and Huffman, *J. Amer. Chem. Soc.*, 1943, **65**, 1620.
[4] Pilcher, *Analyt. Chim. Acta*, 1957, **17**, 144.
[5] Aston, Fink, Tooke, and Cines, *Analyt. Chem.*, 1947, **19**, 218.
[6] Tunnicliff and Stone, *ibid.*, 1955, **27**, 73.
[7] Clarke, Johnston, and de Sorbo, *ibid.*, 1953, **25**, 1156.
[8] Rossini, "Chemical Thermodynamics," Wiley, New York, 1950.

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which the impurity is liquid-soluble solid-insoluble, the solid–liquid equilibrium temperature T is related to the mole-fraction of impurity in the liquid phase, N_2, by $N_2 = A(T_1^* - T)$, where A, the cryoscopic constant of the major component, $= \Delta H_m/RT_1^{*2}$ where ΔH_m is the molar heat of fusion and T_1^* the freezing point for zero impurity. If N_2^s is the mole-fraction of impurity in the total sample and N_2 that in the liquid phase for a fraction r of the sample melted, then $N_2 = N_2^s/r$. Combination of these equations gives, $T = T_1^* - (N_2^s/A)(1/r)$. The mole-fraction of impurity in the sample is obtained from the slope of the plot of T against $(1/r)$ and the intercept at $(1/r) = 0$ gives T_1^*.

The theory depends upon the application of the ideal-solution laws which is reasonable for very pure samples as only dilute solutions of impurity are involved. It is assumed that the impurity is liquid-soluble solid-insoluble. Solid solutions can occur when the impurity has molecular dimensions similar to those of the major component or when the latter has a small heat of fusion, and cause the curve of T against $(1/r)$ to be concave upwards. Mastrangelo and Dornte's treatment can then be used to estimate the impurity.[9]

The limitations of the calorimetric procedure have been discussed by McCullough and Waddington.[10] As the method is essentially a determination of the mole-fraction of impurity, for nearly pure samples a large error in " impurity determination " will result in a small uncertainty in the degree of purity.†

Construction and Operation of the Calorimeter.—The calorimeter E [Fig. 1(*a*)], of internal volume *ca.* 3 ml., consists of the copper portion of a Housekeeper seal ($\frac{1}{2}$ in. o.d. × 1$\frac{1}{2}$ in. closed at the bottom) sealed at A to 16 mm. diam. Pyrex glass. Six thin horizontal copper vanes, silver-soldered to a central wire B, promote temperature equilibrium and prevent solid particles settling during melting. 30 Ohms of 40 S.W.G. copper wire D wound non-inductively on the copper tube acts as resistance thermometer and heater. Temperature changes will not strain the wire as it has the same coefficient of thermal expansion as the calorimeter. The coil, insulated with glyptal varnish and by a layer of " Scotch " electrical insulating tape, is covered with copper foil C to minimise radiation loss. Two leads only are attached.

The calorimeter is surrounded by a copper shield G (1$\frac{1}{4}$ in. i.d. × $\frac{1}{16}$ in. thickness), as a constant-temperature jacket, heated by a winding of 400 ohms (J) of 35 S.W.G. Eureka wire, insulated and covered (K) as above. The shield temperature is measured around its centre with a copper resistance thermometer H of similar characteristics to that of the calorimeter.

The central glass filling tube is covered with a thin copper sheath wound with 400 ohms of 35 S.W.G. Eureka wire M as heater and a third copper resistance thermometer L is placed at its lower end. The tube temperature must be maintained slightly above that of the calorimeter to prevent distillation of the specimen. The calorimeter leads are placed in intimate contact with the shield before being passed up beneath the tube heater. The tube heater is also protected as above and covered with a closely fitting conical tube O (0·2 mm. thickness, copper). The constant-temperature shield is held in position by three stout copper wires N soldered to the conical tube.

The whole assembly P, Q, R, M [Fig. 1] is inside a vacuum-tight glass jacket S (6 cm. i.d. × 40 cm. long) which can be immersed in a cooling bath of liquid nitrogen or solid carbon dioxide–acetone. U is a B55 ground-glass joint, V is a picein seal. Vacuum is applied at Y, and communicates with the calorimeter through holes F.

Temperature Measurement.—The calorimeter, shield, and tube temperatures are obtained from the thermometer resistances [*ca.* 30 ohms at 25°]. No compensation is made for the leads [*ca.* 0·3 ohm] but these will not change significantly during an experiment because they are kept together and are not disturbed. Mercury switches are used to ensure reproducible contact resistances. The error in absolute resistance measurement is assessed at ±0·1 ohm, corresponding to a temperature error of ±1°. Purity determinations, however, require temperature differences, and thus sensitive temperature measurements rather than high absolute accuracy.

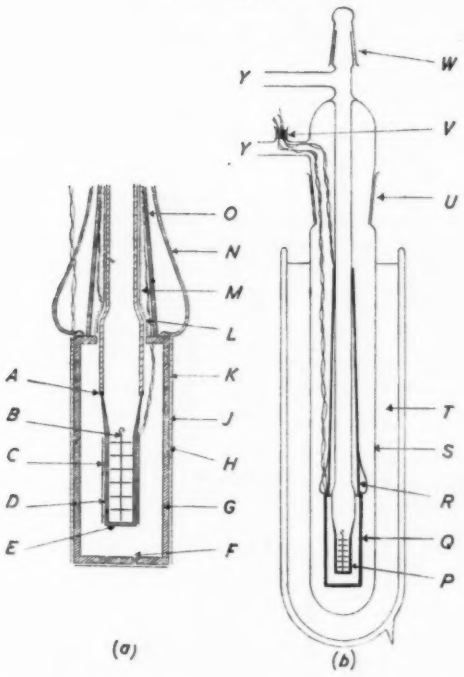
† For a sample of purity 99·9 moles %, a 20% error in " impurity determination " would fix the purity within 99·88 to 99·92 moles %.

[9] Mastrangelo and Dornte, *J. Amer. Chem. Soc.*, 1955, **77**, 6200.
[10] McCullough and Waddington, *Analyt. Chim. Acta*, 1957, **17**, 80.

The thermometer resistances are balanced in a Wheatstone bridge whose measuring arm is two parallel resistances R_1 and R_2; the measured resistance is $R_1R_2/(R_1 + R_2)$. R_1 is a good-quality resistance box, adjustable in 0·1 ohm steps, set 0·1 ohm above the resistance to be measured. R_2, the variable arm of an inexpensive resistance bridge (0—10,000 ohms in 1 ohm steps), is adjusted for balance and kept as large as possible, generally around 2000 ohms when a 1 ohm change in R_2 corresponds to an overall change of $<0·0001$ ohm; thus contact resistance variations in R_2 are negligible. The current through the thermometer coil is *ca.* 2 mA and the heating effect is insignificant. A Cambridge short period galvanometer [25 ohms; 300 mm./μA at 1 m.] is used to detect the balance point and the overall sensitivity of temperature measurement is about 0·0003°.

Electrical Energy Measurement.—The current (i A) through the calorimeter coil is measured with a calibrated milliammeter (0—200 mA) and timed to 0·2 sec. with a stop-clock.

FIG. 1. *Apparatus.*



The coil resistance (R ohms) is taken as the mean of its values at the beginning and end of the heating period (t sec.) because the coil is in good thermal contact with the calorimeter and can be assumed to be always at calorimeter temperature. The electrical energy supplied is then i^2Rt joules and is accurate to about ±1%. The current, from lead storage cells, is adjusted with a variable resistance and a dummy heater which allows the current to become steady before switching to the calorimeter.

Temperature Control of Shield and Tube.—The shield is maintained constant at approximately the m. p. of the sample and the tube about 1° above this, both ±0·05°, which is satisfactory as the thermal leakage between the calorimeter and its environment is small. The current through the heaters, from a stabilised transformer (10—50 v), is controlled by resistances.

Procedure.—A known weight of compound is either distilled *in vacuo* into the calorimeter or injected and then degassed, and measurements are done under its vapour pressure (*i.e.*, triple points are examined). An approximate m. p. can be found from a time–temperature freezing curve or more accurately from the slow-melting curve (with the jacket evacuated and

the shield at about 10° above the calorimeter). From the latter an approximate heat of fusion and degree of purity can be estimated as in ref. 1 (1945).

The solid sample is held about 10° below the m. p. whilst the shield and tube temperatures are adjusted to the required values and these are observed and controlled during the experiment. Calorimeter temperatures are read at 3 min. intervals to establish temperature drifts. Energy inputs are made, at first to determine the effective heat capacity of the calorimeter plus contents and then to melt the sample in stages, the inputs being arranged so that fractions of about $\frac{1}{4}$, $\frac{1}{3}$, $\frac{1}{2}$, and almost unity of the sample are liquid at the end of each stage. The sample is finally melted, the heat capacity again determined, and temperature drift rates remeasured.

The heat-capacity measurements are accurate to about $\pm 3\%$ and a mean value for the

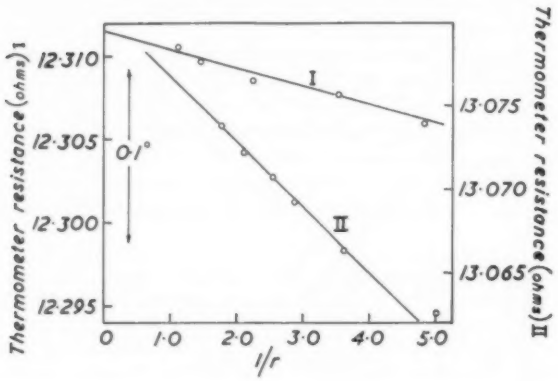


FIG. 2. *Plots for diethyl ether* (*I*; 99·96 ± 0·004 *moles* %) *and tetrahydrofuran* (*II*; 99·87 ± 0·02 *moles* %).

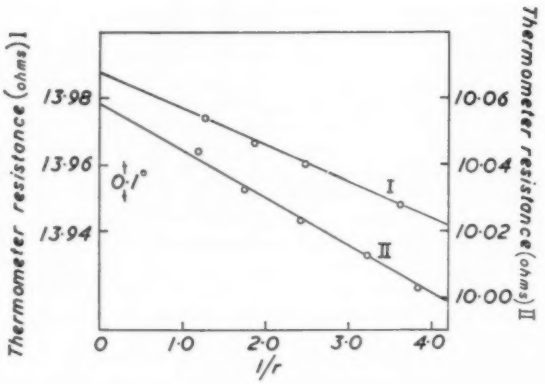


FIG. 3. *Plots for divinyl ether* (*I*; 99·68 ± 0·06 *moles* %) *and hex-1-ene* (*II*; 99·17 ± 0·06 *moles* %).

solid and the liquid state is used in the calculation. From the calorimeter temperature drift rates before and after melting the rate of heat input to the calorimeter from the surroundings can be calculated for intermediate temperatures. This exchange heat input must be added to the electrical energy input to give the total energy absorbed which is distributed between the melting process and the raising of the temperature of the system. The energy absorbed in melting in each stage can then be calculated and from the total heat of fusion the fractions melted obtained. After an electrical-energy input about 10—15 min. must be allowed for the system to regain equilibrium and these temperature equilibrium points are chosen to be the end points of the stages.

Results.—Several classes of compound have been examined. Hex-1-ene, from the National Chemical Laboratory (Standard Sample No. 19-4407) had been found at the National Bureau of Standards, Washington, to be 99·22 ± 0·10 moles % pure, in good agreement with our value, 99·17 ± 0·06 moles %. Diethyl ether (" AnalaR ") was dried over sodium. Remaining

samples were either prepared in this department or obtained commercially and were generally fractionally distilled through a 50 cm. column of Dixon rings. The results are summarised in the Table, which shows that the heat of fusion measured is accurate to *ca.* ±10%, this being satisfactory for calculation of the cryoscopic constant. When a more accurate value for this constant is available it is preferred. Fig. 2 shows some curves of T against $(1/r)$ obtained for samples of high purity and Figs. 3 and 4 for samples of moderate and low purity respectively.

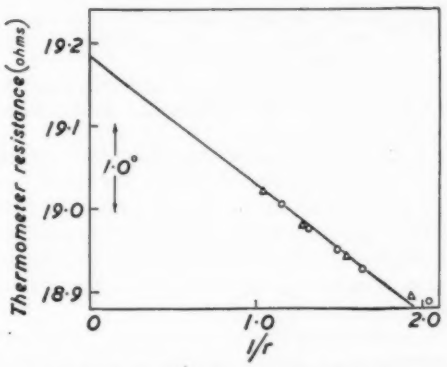


FIG. 4. *Plot for two experiments with trimethylphenyltin* (96·1 ± 0·8 *moles* %).

Because the calorimeter is not adiabatic it is not practicable to start experiments far below the m. p., so for impure samples some may be liquid at the starting temperature. From the mole-fraction on impurity at first obtained the initial fraction melted is calculated and the " observed " heat of fusion and fractions melted corrected. Successive approximations can be made, as for trimethylphenyltin.

Usually the slope can be obtained to ±10%, and thus the molar percentage of impurity to ±10% if the cryoscopic constant is known accurately, otherwise to ±20%. The total time taken is 3—4 hr; this cannot be extended because the calorimeter is not adiabatic. This limits its use, because some substances take a long time for the solid and liquid phases to reach thermodynamic equilibrium, particularly when the latter is very viscous. No such difficulties were encountered with the above compounds.

Compound	M. p.	ΔH_m (cal. mole^{-1}) Obs.	Lit.	A (deg.$^{-1}$)	Purity (moles %)
Hex-1-ene	−140°	2200 ± 200	2234 [a]	0·06318	99·17 ± 0·06
Trimethylene oxide	−97	1550 ± 150		0·025	99·81 ± 0·04
Furan	−86	890 ± 100	908·8 ± 0·2 [b]	0·01301	99·78 ± 0·02
Tetrahydrofuran	−109	2175 ± 200		0·040	99·87 ± 0·02
Tetrahydropyran	−49	425 ± 50		0·0039	99·81 ± 0·04
Diethyl ether	−116	1650 ± 150	1745 [c]	0·036	99·96 ± 0·004
Divinyl ether	−100	1900 ± 200		0·032	99·68 ± 0·06
Benzonitrile	−14	2170 ± 200		0·016	99·24 ± 0·15
Bicyclo[2,2,1]heptadiene	−68	1670 ± 150		0·020	99·34 ± 0·10
Trimethylphenyltin	−51	2410 ± 200		0·025	96·1 ± 0·8

[a] McCullough, Finke, Gross, Messerly, and Waddington, *J. Phys. Chem.*, 1957, **61**, 289. [b] Guthrie, Scott, Hubbard, Katz, McCullough, Gross, Williamson, and Waddington, *J. Amer. Chem. Soc.*, 1952, **74**, 4662. [c] Parks and Huffman, *ibid.*, 1926, **48**, 2788.

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297. *The Enzymic Synthesis and Degradation of Starch. Part XXIV.* The Purification of D- and Q-Enzymes.*

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Details are given of a method for the isolation of D-enzyme and Q-enzyme from the same sample of potato juice. Both enzyme preparations are free from amylases and phosphorylase, and neither contains a detectable amount of the other.

It is established that Q-enzyme, when free from D-enzyme, exerts no appreciable " transferase " action on natural amylopectin.

In a previous communication [1] we described the preparation of D-enzyme from the potato. This enzyme preparation was free from phosphorylase but contained traces of other carbohydrases, notably Q-enzyme. These impurities were of little consequence in many studies but interfered with experiments designed to elucidate the mode of action of D-enzyme. Further methods of purification have now been developed and this communication describes the method finally adopted to give a purified D-enzyme and, at the same time, a purified Q-enzyme.

Baum and Gilbert [2] used partly retrograded amylose suspensions as adsorbents for phosphorylase and Q-enzyme in the purification of these two enzymes and found that in the presence of 11% (w/v) ethanol, the Q-enzyme of potato juice was quantitatively adsorbed on the amylose. When the amylose precipitate was washed with buffer solution a portion of the Q-enzyme was eluted. The remainder, however, was more firmly held and could be eluted only by the natural substrate, starch or its components, dissolved in water.[2,3] No details being available, the study of the behaviour of D-enzyme under these conditions was undertaken. As starting material we have used (*a*) charcoal-clarified potato juice [1] and (*b*) the enzyme mixture obtained from the juice by precipitation with ammonium sulphate in presence of copper sulphate (to inactivate phosphorylase [4]). As in Baum and Gilbert's work [2,3] each preparation (*a*) and (*b*) was treated first with 0·15% and then with 0·3% amylose suspensions to give precipitates A and B respectively, from which the enzymes were recovered by elution with buffer.[2,5] Table 1 shows that, with each starting material, *a* and *b*, 70—80% of the D-enzyme was recovered from precipitate A and none from precipitate B.

Table 1. *Adsorption of potato enzymes on retrograded amylose.*

	Recovery as % of original activity			
	(*a*) Charcoal-clarified juice		(*b*) Juice precipitated with ammonium sulphate	
Enzyme	Precipitate A	Precipitate B	Precipitate A	Precipitate B
Q-Enzyme	21	5	13	0
D-Enzyme	70	0	78	0
Phosphorylase	10	70	0	0
Amylase	5	5	0	0
R-Enzyme	0	0	0	0

The eluate from precipitate A also contained 10—20% of the Q-enzyme (together with traces of other enzymes when charcoal-clarified juice, *a*, was used).

While this method gave considerable purification of D-enzyme with respect to protein

* Part XXIII, *J.*, 1957, 2490.

[1] Peat, Whelan, and Rees, *J.*, 1956, 44.
[2] Baum and Gilbert, *Nature*, 1953, 171, 983.
[3] Baum, Ph.D. Thesis, Birmingham, 1953.
[4] Peat, Whelan, and Jones, *J.*, 1957, 2490.
[5] Whelan, " Methods in Enzymology," Vol. I, Academic Press, New York, 1955, p. 194.

and other enzymes, it did not give a product free from Q-enzyme. Consequently we directed our attention towards the fraction of the D-enzyme (20—30%) which was not eluted from the amylose by buffer.

Inasmuch as firmly adsorbed Q-enzyme is eluted by solutions of its substrate,[2,3] it was argued that the firmly held D-enzyme might be desorbed by a solution of maltodextrins of low molecular weight which would not be expected to desorb the firmly bound Q-enzyme since they are not substrates for the latter enzyme. The D- and the Q-enzyme of potato juice were therefore adsorbed on amylose, and the loosely held fractions removed by elution with buffer solution. The amylose residue was then extracted with 0·05% maltotriose dissolved in buffer solution (pH 7·0), and the extracts were examined for D- and Q-enzyme activities. The extract contained 18% of the original D-enzyme activity of the potato juice but no detectable Q-enzyme. After dialysis to remove maltotriose, the D-enzyme was precipitated with ammonium sulphate, redissolved in citrate buffer solution, and freeze-dried.

The amylose precipitate left after extraction of the D-enzyme still held the strongly adsorbed fraction of Q-enzyme and we have confirmed that this fraction can be extracted by dilute solutions of starch or starch components.[2] Q-Enzyme obtained in this way is free from D-enzyme, but if the extraction with maltotriose is omitted both D- and Q-enzymes are eluted together.

Properties of Purified D-Enzyme.—The enzyme prepared as described could be stored for periods of at least 3 months without loss of activity. It was free from detectable amounts of amylases, Q-enzyme, or phosphorylase. It appeared to be without action, as judged by diminution of intensity of iodine stain (A.V.)[6] or by liberation of reducing groups, on either of the separated components of starch, amylose, and amylopectin. It is not, however, to be expected that the transfer by D-enzyme of a fragment of one amylose chain to another would become manifest by either a fall of A.V. or an increase in reducing power. If an acceptor such as glucose is present, the transferring action of D-enzyme is at once detected by a diminution of A.V. Despite the failure of these methods to detect an action of D-enzyme on amylose or amylopectin, separately, nevertheless when whole potato starch was used as the substrate, a fall in blue value[6] was observed from 0·44 to a constant value of 0·29 in 25 hr. It may be that the difference is ascribable to the transfer in whole starch of amylose fragments to the non-reducing ends of the amylopectin, with a consequent diminution of A.V. It is perhaps worthy of note that no change of reducing power is observed in the action of D-enzyme on whole starch.

Properties of Purified Q-Enzyme.—The enzyme prepared as described is free from D-enzyme, phosphorylase, and amylases. We confirm the unpublished observation by Dr. G. A. Gilbert that the purified Q-enzyme is best stored as the enzyme–amylose complex which is freeze-dried and can be reconstituted when required. With this preparation we have reinvestigated the action of Q-enzyme on amylopectin.

Although it is generally agreed that the rapid action of Q-enzyme on amylose ceases when a branched polysaccharide similar to natural amylopectin is produced, it is by no means established that Q-enzyme has any action on natural amylopectin. Most of the Q-enzyme preparations previously obtained have in fact exhibited a slow action on amylopectins, manifested by a diminution in intensity of the iodine stain of the substrate.[7,8] Larner[8] has shown that Q-enzyme preparations exert a branching action on synthetic polysaccharides which in respect of the length of the outer chains are amylopectins in type. At the same time is was claimed that the amylopectin of maize was attacked by Q-enzyme. It may be premature to ascribe this slow action on amylopectin specifically to Q-enzyme since it is now known that the earlier preparations contained D-enzyme in addition.

[6] Bourne, Haworth, Macey, and Peat, *J.*, 1948, 924.
[7] Barker, Bourne, and Peat, *J.*, 1949, 1712; Peat, Whelan, and Bailey, *J.*, 1953, 1422; Rees, Ph.D. Thesis, Cambridge, 1953.
[8] Larner, *J. Biol. Chem.*, 1953, **202**, 492.

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Q-Enzyme was extracted from the amylose precipitate with a dilute solution of waxy-maize amylopectin and the extract added to a digest containing a sample of the same amylopectin. There appeared to be no effect on the amylopectin as judged by iodine stain in the course of 48 hr. In a similar experiment with potato amylopectin there was no change in the iodine stain during 60 hr. although tests indicated that the enzyme was still active. Estimation, by periodate oxidation, of the basal chain length (proportion of non-reducing end glucose units) of the potato amylopectin at intervals during this experiment gave the results listed in Table 2. The decrease in chain length is so small

TABLE 2. *Action of Q-enzyme on potato amylopectin.*

Time (hr.)	0	12	24	60	96	108
A.V.*	18·0	18·0		17·9		
Chain length †	26·0		26·2	25·2	25·2	24·4

* Intensity of iodine stain measured in arbitrary units [1] with an E.E.L. colorimeter. † By periodate oxidation.

over the prolonged incubation period that it is reasonable to conclude that Q-enzyme has no appreciable " transferase " action on natural amylopectin.

EXPERIMENTAL

General Methods.—Starch fractions were prepared as by Hobson *et al.*[9] For estimation of reducing sugars, blue value (B.V.), and absorption value (A.V.), see Bourne *et al.*[6] In the isolation of enzymes, all operations were performed at 0°, with reagents previously cooled to 0°. Periodate oxidation of polysaccharides was carried out on samples (50 mg.) dissolved in 3% (w/v) sodium chloride (10 ml.) with 0·37M-sodium metaperiodate (10 ml.). The formic acid produced was estimated by the micro-method of Peat *et al.*[10] Charcoal-clarified potato juice was prepared as by Peat *et al.*[1] and phosphorylase-free enzymes were prepared from this juice by precipitation with ammonium sulphate in presence of copper sulphate as by Peat *et al.*,[4] and redissolution in 0·01M-citrate buffer (pH 7·0).

Measurement of Activity of Enzymes.—(i) For D-enzyme, two methods were used. (*a*) A maltodextrin mixture was prepared and fractionated on a charcoal–Celite column as by Whelan *et al.*[11] The fractions eluted from the column between 20% and 50% (v/v) ethanol were pooled and evaporated to dryness. The maltodextrin mixture so obtained had maltotetraose as its lowest member. The digest in an E.E.L. colorimeter cell (1·3 cm.) contained 4% (w/v) of maltodextrin (0·1 ml.) and enzyme solution (0·1 ml.) and was incubated at 35° for 30 min. Iodine solution (7 ml., containing 5 mg. of iodine and 25 mg. of potassium iodide per 100 ml.) was added, and the iodine stain measured in the E.E.L. colorimeter at 510 mμ (Ilford filter No. 404). A digest containing no enzyme was used as control. The increase in the iodine stain was taken as a measure of activity. (*b*) Two digests, each containing 1% (w/v) of waxy-maize amylopectin (1 ml.), 0·2M-citrate buffer (pH 7·0; 2 ml.) and enzyme solution (2 ml.), were prepared. Glucose (20 mg.) was dissolved in one digest, and both were incubated at 20°. After 30 min. samples (1 ml. each) were withdrawn and stained with iodine (2 mg.) and potassium iodide (40 mg.) in a final volume of 50 ml., and the absorption values measured at 680 mμ. The difference in A.V. between the two digests was used as a measure of D-enzyme activity. (ii) Q-Enzyme and α-amylase were determined as by Gilbert and Patrick.[12] Qualitative tests for Q-enzyme activity were made by comparing visually the iodine stains at the beginning and after digestion for 30 min. A perceptible change of the stain towards red was taken as evidence of activity provided that no amylase was present. (iii) Phosphorylase was determined by Whelan and Bailey's method [13] and (iv) R-enzyme was detected by its action on amylopectin.[14]

[9] Hobson, Pirt, Whelan, and Peat, *J.*, 1951, 801.
[10] Peat, Whelan, and Turvey, *J.*, 1956, 2317.
[11] Whelan, Bailey, and Roberts, *J.*, 1953, 1293.
[12] Gilbert and Patrick, *Biochem. J.*, 1953, **51**, 181.
[13] Whelan and Bailey, *Biochem. J.*, 1954, **58**, 560.
[14] Hobson, Whelan, and Peat, *J.*, 1951, 1451.

Adsorption of Potato Enzymes on Retrograded Amylose.—Butanol–amylose complex,[5] equivalent to 0·5 g. of amylose, was dissolved in water (200 ml.) and boiled until the volume was reduced to 100 ml. After cooling, 0·5M-citrate buffer (pH 6·0; 2 ml.) was added, and the solution cooled slowly to 0° with constant stirring. The retrograded amylose appeared as a flocculent suspension which was used directly for the adsorption of enzymes. For the preparation of " 50% ethanol " and " 11% ethanol " see Whelan.[5]

The charcoal-clarified potato juice (50 ml.) was adjusted to pH 6·0 with 0·1N-hydrochloric acid and then brought to 11% (w/v) ethanol concentration by addition of " 50% ethanol." It was then poured slowly, with stirring, into amylose suspension (15 ml.), and the ethanol concentration readjusted to 11% by addition of " 50% ethanol." After 15 minutes' stirring the amylose precipitate (precipitate A) was separated on the centrifuge and washed three times with portions (100 ml. each) of " 11% ethanol." The loosely bound enzymes were finally extracted from precipitate A by gently stirring it for 15 min. with 0·05M-citrate buffer (pH 7·0; 25 ml.), centrifuging the mixture, and filtering the supernatant solution through a grade 3 sintered-glass filter. The residue was similarly extracted with a second portion of buffer, and the extracts were combined for determination of enzyme activities (Table 1). The solution remaining after removal of precipitate A was added slowly to a further quantity of the amylose suspension (125 ml.), and the ethanol concentration again adjusted to 11%. After 15 minutes' stirring the mixture was separated on the centrifuge to give precipitate B. This precipitate was washed and the enzymes were extracted as for precipitate A.

The enzyme solution (50 ml.) obtained from potato juice by precipitation with ammonium sulphate was submitted to the same procedure, and the recovery of enzyme activity determined (Table 1).

Elution of firmly Bound Enzymes from Retrograded Amylose.—Potato juice (200 ml.) was precipitated with ammonium sulphate and redissolved in 0·01M-citrate buffer (pH 6·0; 150 ml.) as described above. The enzymes were then adsorbed on to retrograded amylose (0·5 ml. per ml. of enzyme solution) in presence of " 11% ethanol," as in the preceding experiment, to give precipitate A which was washed five times with portions (250 ml. each) of " 11% ethanol." Precipitate A was then extracted with five portions (30 ml. each) of 0·05M-citrate buffer (pH 7·0) to remove loosely bound enzymes. Only the first three extracts were active, containing Q-enzyme and 74% of the original D-enzyme activity of the potato juice. The residual precipitate was then eluted four times with portions (30 ml. each) of 0·05% (w/v) maltotriose in 0·05M-citrate buffer (pH 7·0), and the extracts were filtered through a grade 4 sintered-glass filter and tested for enzymic activity. Extracts 1 and 2 contained 11% and 8% respectively of the original D-enzyme activity, and extracts 3 and 4 were inactive. No Q-enzyme, R-enzyme, or α-amylase could be detected in any of these extracts.

The amylose precipitate A remaining after elution of the D-enzyme was extracted with 0·05% (w/v) potato amylose (blue value 1·45) in 0·05M-citrate buffer (pH 7·0; 20 ml.). After centrifugation and filtration through sintered glass, the extract was incubated at 20° and portions (0·5 ml. each) were removed at intervals and examined for Q-enzyme activity by measurement of absorption value (680 mμ) after staining with iodine (1 mg.) and potassium iodide (10 mg.) in a total volume of 50 ml.:

Time of incubation at 20° (hr.)	0	1	2·5	4	25
A.V. (680 mμ)	0·555	0·120	0·050	0·049	0·049

There was no detectable D-enzyme or α-amylase activity.

In a similar experiment in which the extraction with maltotriose was omitted, the extract obtained with amylose solution contained both D- and Q-enzyme.

Final Method Adopted for Preparation of D- and Q-Enzyme.—The enzyme solution (150—200 ml.) obtained by precipitation of potato juice with ammonium sulphate in the presence of copper sulphate was treated with " 50% ethanol " and amylose suspension (0·3 ml. per ml. of enzyme solution) as described above, to give precipitate A. The precipitate was washed and loosely adsorbed enzymes were extracted with citrate buffer as in the preceding experiment. D-Enzyme was extracted from the residual amylose precipitate A with four portions (20 ml. each) of 0·05% (w/v) maltotriose in 0·05M-citrate buffer (pH 7·0). The first two extracts were filtered and dialysed against three changes of 0·05M-citrate buffer (pH 7·0; 1 l.) for 24 hr. To the impermeate solution was added 50% (w/v) ammonium sulphate (pH 7·0) to a final concentration of 23% (w/v), and the precipitate removed on a grade 4 filter and washed on the filter

with a mixture of 50% (w/v) ammonium sulphate (pH 7·0; 1 vol.) and 0·05M-citrate buffer (pH 7·0; 1 vol.). The precipitate was dissolved in 0·05M-citrate buffer (pH 7·0; 10 ml.) and freeze-dried. The product usually contained 10—15% of the original D-enzyme activity. After the removal of D-enzyme, precipitate A was suspended in 0·05M-citrate buffer (pH 7·0; 50 ml.) and freeze-dried. The freeze-dried product was stored at 0° over phosphoric oxide until required for elution of the Q-enzyme. In this form the Q-enzyme remained active for periods up to 3 months.

Action of D Enzyme on Starch Fractions.—Each digest contained 0·2M-citrate buffer (pH 7·0; 3 ml.), D-enzyme solution (2 ml.), and polysaccharide solution (5 ml.). The polysaccharide solutions were: 0·1% (w/v) potato amylose (B.V. 1·45); 0·5% (w/v) waxy-maize amylopectin; and 0·4% (w/v) potato starch (B.D.H. soluble starch). After incubation at 20° for various times, portions (1 ml. each, but 0·5 ml. for potato starch) were removed and stained with iodine (1 mg.) and potassium iodide (10 mg.) in 100 ml., and the absorption values were measured at 680 mμ. The absorption values of the amylose and amylopectin digests remained constant at 0·720 and 0·372 respectively during 24 hr., while that of the potato starch underwent the following changes:

Time (hr.)	0	2	4	7	20	25
A.V. (680 mμ)	0·440	0·412	0·376	0·348	0·291	0·290

No reducing sugars were detected in any digest.

Action of Q-Enzyme on Amylopectins.—(i) *Waxy-maize amylopectin.* The amylose precipitate from 200 ml. of potato juice was extracted, after elution of D-enzyme, with 0·1% (w/v) waxy-maize amylopectin in 0·05M-citrate buffer (pH 7·0; 20 ml.), and the extracts were centrifuged and filtered to remove amylose particles. Qualitative tests on a portion (0·5 ml.) of the extract showed considerable Q-enzyme activity. The bulk of the extract was then added to a 0·25% (w/v) solution (30 ml.) of the same specimen of amylopectin and incubated at 20°. Portions (2 ml. each) were removed at intervals and stained with iodine (2 mg.) and potassium iodide (20 mg.) in a final volume of 100 ml. and the absorption values measured at 680 mμ. The absorption value remained constant at 0·210 during 48 hr.

(ii) *Potato amylopectin.* The Q-enzyme was extracted from an amylose precipitate with 0·1% (w/v) potato amylopectin in citrate buffer (25 ml.) as described above. Qualitative tests having indicated Q-enzyme activity, the extract (20 ml.) was added to a digest containing potato amylopectin (505 mg.; 100 ml.) and 0·05M-citrate buffer (pH 7·0; 25 ml.) and incubated under toluene at 20°. Portions (0·5 ml. each) were removed at intervals and stained with iodine as described and the absorption values were measured in the E.E.L. colorimeter with 1·3 cm. cells and Ilford filter No. 608 (peak transmission at 680 mμ). Portions (2 ml. each) of the digest were also removed at 60 hr. and 108 hr. for qualitative tests of Q-enzyme activity. In both cases the enzyme was still highly active. Further portions (30 ml. each) were removed at intervals, boiled for 5 min., cooled, and dialysed at 2° for 4 days against running distilled water. The impermeate solutions were freeze-dried, and the recovered polysaccharides dried to constant weight at 60°. Portions (50 mg. each) of the polysaccharides were subjected to periodate oxidation (Table 2).

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298. *The Mesomorphic Transition Temperatures of 3′-Substituted 4′-n-Octyloxydiphenyl-4-carboxylic Acids.*

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The preparation of 3′-fluoro- and -iodo-4′-*n*-octyloxydiphenyl-4-carboxylic acids now makes it possible to compare the relative effects of 3′-H-, -F-, -Cl-, -Br-, -I-, and -NO_2-substituents upon the mesomorphic transition temperatures. The nematic–isotropic transition temperatures decrease quite regularly with increasing molecular breadth, but such a relationship does not hold for the smectic–nematic transition temperatures. These temperatures appear to be sensitive to change in the permanent polarisation of the molecule, and this, together with the change in molecular breadth, must be taken into account in assessing smectic–nematic transition temperatures.

The 4′-*n*-alkoxydiphenyl-4-carboxylic acids [1] are suitable parent compounds for a study of the relative effects of substituents on the thermal stabilities of mesophases. They exhibit enantiotropic mesophases with high transition temperatures which are well separated from the melting points (solid–mesophase transition), and therefore the introduction of even bulky substituents does not eliminate the mesomorphic properties (cf. 4-*n*-alkoxy-3-bromobenzoic acids [2] which are not mesomorphic). The 3′-chloro-, -bromo-, and -nitro-derivatives [3] of these diphenyl acids have already been studied, but to establish the relative effects of the substituents F, Cl, Br, I, and NO_2 upon the mesomorphic properties of one particular molecule type, the 3′-fluoro- and -iodo-4′-*n*-octyloxydiphenyl-4-carboxylic acids have now been prepared. Synthetical difficulties prevented our studying a homologous series of ethers, as was possible for the chloro-, bromo-, and nitro-compounds. However, existing data show that comparisons of the transition temperatures for one particular ether or of the average transition temperatures for several ethers do not lead to substantially different results. The smectic–nematic and nematic–isotropic transition temperatures for the octyl ethers in Table 1 are therefore a reliable guide to the relative influences of the substituents on the smectic and nematic thermal stabilities.

Table 1. 3′-X-4′-n-*Octyloxydiphenyl-4-carboxylic acids.*

X	H	F	Cl	Br	I	NO_2
Smectic–nematic transition temp.	255°	254·5°	225°	214°	192·5°	214° *
Decrease in transition temp. from unsubstituted acid		0·5	30	41	62·5	41
Nematic–isotropic transition temp.	264·5	255·5	233	224	214	214 *
Decrease in transition temp. from unsubstituted acid		9	31·5	40·5	50·5	50·5

* Smectic–isotropic transition temperature.

The octyl ether of the 3′-nitro-derivative exhibits no nematic mesophase, and the smectic–isotropic transition temperature, 214°, has been used in both sets of figures in the Table. This transition temperature may be compared with the other smectic–nematic transition temperatures, and the order of increasing effect of the substituents on the thermal stability of the smectic mesophase for 4′-*n*-octyloxydiphenyl-4-carboxylic acid is $H < F < Cl < Br = NO_2 < I$. At first sight, the smectic–isotropic transition temperature for $X = NO_2$ should not be comparable with the nematic–isotropic transition temperatures for the other derivatives. However, when nematic properties cease to appear at a particular member in a homologous series, the smectic–nematic and nematic–isotropic transition temperature curves coincide, *i.e.*, the smectic–isotropic curve is a

[1] Gray, Hartley, and Jones, *J.*, 1955, 1412.
[2] Gray and Jones, *J.*, 1954, 2556.
[3] Gray, Jones, and Marson, *J.*, 1957, 393.

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continuation of the nematic–isotropic curve. Regarded in this way, smectic–isotropic and nematic–isotropic transition temperatures may be compared, and the order of increasing effect of the substituents upon the nematic thermal stability of 4′-*n*-octyloxydiphenyl-4-carboxylic acid is H < F < Cl < Br < I = NO_2. In support of this sequence, the order obtained for X = H, Cl, Br, and NO_2 by comparing average *nematic*–isotropic transition temperatures (*e.g.*, for the propyl–hexyl ethers) is H < Cl < Br < NO_2.

The nitro-group has a smaller effect upon the thermal stability of the smectic mesophase than on that of the nematic mesophase, probably [3] owing to the large C–NO_2 dipole moment which counteracts the separation of the molecular axes arising from the bulk of the nitro-group. In an attempt to assess the effect of substituent size upon the two mesophase types, the minimum overall molecular breadths (defined as the diameter of the smallest cylinder through which the dimerised aromatic carboxylic acid would pass, the flexible alkyl chain being assumed not to interfere) of the 3′-substituted diphenyl acid dimers have been calculated. These breadths (*R*) are plotted against the nematic and

FIG. 1*a*.

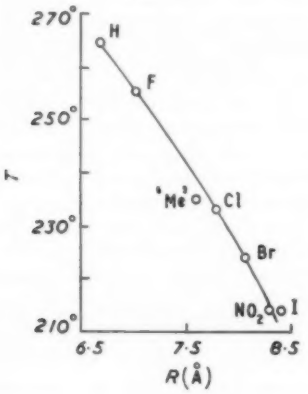
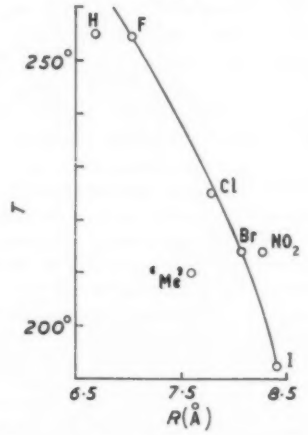


FIG. 1*b*.

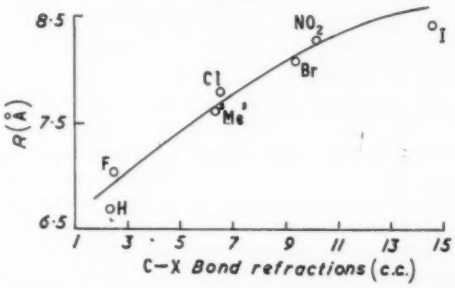


smectic transition temperatures (*T*) in Figs. 1*a* and 1*b*. For the nematic transitions (Fig. 1*a*), the transition temperatures decrease reasonably smoothly with increasing molecular breadth, and it appears that the order H < F < Cl < Br < I = NO_2 is determined largely by the separation of the molecular axes. Unfortunately, the pure 3′-methyl acid is not available, but in seven cases in which analogous mesomorphic methyl- and chloro-substituted compounds have been examined, the average increase in nematic–isotropic transition temperature from chloro- to methyl derivative is about 2°. This leads to a predicted nematic–isotropic transition temperature of 235° for 3′-methyl-4′-*n*-octyloxydiphenyl-4-carboxylic acid. Using a breadth (*R*) of 7·6 Å for this molecule, we obtain a point close to the curve in Fig. 1*a*. It is particularly significant that the point for X = NO_2 lies so close to the curve, *i.e.*, the large C–NO_2 dipole moment appears to have little influence upon the thermal stability of the nematic mesophase. Thus, molecular interactions of the dipole–dipole or induced dipole type do not appear to contribute significantly to the intermolecular attractions in the nematic mesophase. Dispersion forces, arising from molecular polarisability, must therefore account for the molecular interactions which maintain the parallel orientation of the molecules in the nematic state. The gas-phase relation being assumed to hold, the energy of interaction for these forces is proportional to (molecular polarisability)^2/(molecular separation).[6] As the separation of the molecular axes increases, the interaction energy will fall off rapidly (cf. the increasing gradient of the curve in Fig 1*a* with increasing *R*). The molecular polarisabilities will

interfere with a smooth-curve relationship between T and R only if the polarisabilities change in an irregular way with increasing substituent size. In fact, Fig. 2 shows that the C–X bond refractions increase fairly regularly with increasing R. Therefore the increases in polarisability with change in substituent X will merely reduce the gradient of the curve in Fig. 1*a*.

Fig. 1*b* shows that the relation between the smectic–nematic transition temperatures and the molecular breadths is not simple. Thus, X = F has a small effect upon the thermal stability of the mesophase, and the breadth increase must be counteracted by the increase in intermolecular interaction arising from the increase in permanent polarisation on passing from X = H to X = F. The points for X = F, Cl, Br, and I lie on a curve, presumably because no large fluctuation in dipole moment occurs along this sequence. However, with X = NO_2, the point is displaced from this curve by some 13°, and the higher thermal stability may be explained by the large C–NO_2 dipole moment. Data on

FIG. 2.



the smectic thermal stabilities of methyl compounds are limited, but from other analogous methyl and chloro-compounds, an approximate smectic–nematic transition temperature of 210° would be predicted for 3'-methyl-4'-*n*-octyloxydiphenyl-4-carboxylic acid. This point would lie below the above curve by some 23°, explained in this case by the small C–CH_3 dipole moment.

It appears that in the smectic mesophase, the intermolecular attractions arising from dispersion forces are supplemented by dipolar attractions, *i.e.*, by dipole–dipole and induced dipole interactions. That is, the thermal stability of a mesophase will be reduced by substitution which leads to an increase in molecular breadth, but this effect will be counteracted for both mesophase types by the increased polarisability of the substituted molecules, and in the case of the smectic mesophase only, by the substituent's dipole moment. These facts are understandable in terms of the generally accepted molecular orientations in the mesophases. Thus, in the smectic mesophase the molecules are arranged parallel to one another, in layers, since this arrangement gives rise to a strong attraction between the dipoles which operate across the long axes of smectogenic molecules. At the smectic–nematic transition, thermal effects increase the intermolecular separation and weaken these dipolar attractions sufficiently for the molecules to slide out of the layers in the direction of their long axes, whilst retaining the overall parallel orientation. Thus, in the nematic mesophase the ends of the molecules are arranged randomly, so it is less probable that dipoles acting across the molecular axes will lie sufficiently close to give rise to any attraction. Moreover, if, as is often the case, there are two such dipoles acting in opposite directions at opposite ends of the molecule, it is likely that the dipoles in neighbouring molecules will lead to repulsion as often as to attraction, so resulting in a low, overall, average dipole interaction. Such considerations would explain the apparent unimportance of permanent dipoles in relation to the nematic mesophase.

These results cannot be confirmed by reference to other series of substituted mesomorphic compounds. Thus, the 4-*n*-alkoxy-3-bromo-, -iodo- and -nitro-benzoic acids

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and the *trans*-4-*n*-alkoxy-3-iodo- and -nitro-cinnamic acids are not mesomorphic, and in the 5-substituted 6-*n*-alkoxy-2-naphthoic acids [4] the behaviour is anomalous because of the protection of the 5-substituent by the 8-H atom. It would however seem worth while to study the effect of introducing substituents of diverse size and polarity into given systems in order to verify these ideas, since attempts to realise quantitative relationships between mesomorphic and molecular properties would be assisted by this knowledge of the particular types of molecular interaction operating in given mesophase types.

Finally, the purely smectic propyl 3′-fluoro-4′-*n*-octyloxydiphenyl-4-carboxylate has been made, and has a smectic–isotropic transition temperature of 59·5°. The analogous chloro-compound is not mesomorphic, but the 3′-nitro-ester has a smectic–isotropic transition at 47°. Here again, the large C–NO_2 dipole moment is giving rise to a higher transition temperature than would be expected.

It is interesting to record the variations in the decreases in smectic mesophase thermal stability, ΔT(H–X), for a given substituent in different systems. ΔT(H–F) for propyl 3′-substituted-4′-alkoxydiphenyl-4-carboxylates is 43·5°, for 3-substituted-4-alkoxybenzoic acids 10°, and for 3′-substituted-4′-alkoxydiphenyl-4-carboxylic acids 0·5°. Such variations are expected, since on passing from X = H to X = F the increase in intermolecular attraction due to the larger C–F dipole and the greater polarisability of the substituted molecule will depend on the total polarisability of the individual molecules. Indeed, the greater the molecular polarisability, the larger will be the increase in intermolecular attraction due to both induced dipole attraction and dispersion forces, and the smaller will be the overall effect of a substituent in decreasing the smectic thermal stability. This is borne out by the above figures, the three compound types being arranged in order of increasing molecular polarisability (the acids are dimeric). Since dipoles are less important in the nematic mesophase, these arguments will apply then only to the dispersion forces, and there should be less fluctuation in the ΔT(H–X) figures for nematic–isotropic transitions for a given substituent: ΔT(H–F) for 3-substituted-4-alkoxybenzoic acids is 25·5°, and for 3′-substituted-4′-alkoxydiphenyl-4-carboxylic acids is 9°.

Experimental

M. p.s are corrected for exposed stem. Light petroleum had b. p. 40—60°.

Determination of Transition Temperatures.—The m. p.s and mesomorphic transition temperatures were determined in the usual way with an electrically heated microscope block [5] in conjunction with a projection system.[6]

Materials.—Attempts to iodinate the 4′-alkoxydiphenyl-4-carboxylic acids had limited success, since with increasing length of the alkyl chain the amount of un-iodinated material increased, and only in the case of the methyl ether was a reasonable yield of the pure iodo-derivative obtained. Moreover, the methyl ether could not be demethylated without loss of iodine, and 4′-hydroxydiphenyl-4-carboxylic acid could not be restricted to mono-iodination. Several of the longer-chain 4′-alkoxy-3′-nitrodiphenyl-4-carboxylic acids [3] were catalytically reduced to the amines and attempts to replace the amino-group by iodine were made. Although the products were repeatedly crystallised and chromatography on alumina was used, pure compounds could not be isolated. It was therefore decided to prepare 3′-iodo-4′-*n*-octyloxydiphenyl-4-carboxylic acid *via* its ester by carrying out an *N*-nitrosoacetylation between 3-iodo-4-*n*-octyloxyacetanilide and methyl benzoate. This method was successful and was also applied to the preparation of the analogous 3′-fluoro-derivative.

3′-Iodo-4′-methoxydiphenyl-4-carboxylic Acid.—The parent acid (1 mol.) was dissolved in ethanol–concentrated sulphuric acid (4 : 1; v/v) at 40—50°. Iodine (3 mol.) and yellow mercuric oxide (3 mol.) were added and the mixture stirred for 10 hr. at 40—50°. Inorganic matter was filtered off, and the product obtained on dilution of the filtrate was hydrolysed by refluxing it for 90 min. with 2N-ethanolic potassium hydroxide. The hydrolysate was diluted and acidified, and the product was filtered off and crystallised three times from glacial acetic

[4] Gray and Jones, *J.*, 1955, 236.
[5] Gray, *Nature*, 1953, **172**, 1137.
[6] Gray and Ibbotson, *Nature*, 1955, **176**, 1160.

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acid and once from ethanol to give the colourless **3′-*iodo*-4′-*methoxydiphenyl*-4-*carboxylic acid***, m. p. 271·5° (73%) (Found: C, 47·7; H, 3·6; I, 35·6. $C_{14}H_{11}O_3I$ requires C, 47·4; H, 3·2; I, 35·8%).

1-*Iodo*-2-n-*octyloxybenzene*.—*o*-Iodophenol (110 g., 0·5 mole) in absolute ethyl alcohol (300 ml.) containing sodium (11·5 g., 0·5 g.-atom) and *n*-octyl iodide (132 g., 0·505 mole), was refluxed for 12 hr. About one half of the alcohol was distilled off, and the residue poured into water (500 ml.). The carbon tetrachloride extract of the oily ether was washed thoroughly with aqueous sodium hydroxide, then with water, and dried. Removal of solvent under reduced pressure gave 119·5 g. (72%) of 1-*iodo*-2-n-*octyloxybenzene*, b. p. 143—145°/1 mm. (Found: I, 38·0. $C_{14}H_{21}OI$ requires I, 38·2%).

2-*Iodo*-4-*nitro*-1-n-*octyloxybenzene*.—(a) *By nitration*. 2-Iodo-1-*n*-octyloxybenzene (33·2 g., 0·1 mole) was added dropwise during 25 min. to a stirred mixture of glacial acetic acid (125 ml.) and fuming nitric acid (125 ml., *d* 1·5) maintained at 0° ± 1°. A pale yellow solid began to separate 5 min. after commencing the addition. When all the iodo-compound had been added, the mixture was stirred for 5 min. and poured into water (500 ml.). The pale yellow solid was filtered off, washed with 2N-sodium hydroxide and with water, and dried in a vacuum desiccator. Crystallisation from light petroleum gave pale yellow prisms, 27 g. (71·5%), m. p. 48—50·5°. Two further crystallisations from the same solvent gave pure 2-*iodo*-4-*nitro*-1-n-*octyloxybenzene*, m. p. 50·5—51° (Found: C, 44·9; H, 5·7; N, 3·4; I, 34·1. $C_{14}H_{20}O_3NI$ requires C, 44·6; H, 5·3; N, 3·7; I, 33·7%).

(b) *By alkylation*. 2-Iodo-4-nitrophenol [7] was octylated by the general procedure for alkylating *p*-hydroxybenzaldehyde.[8] The solid residue after removal of the *cyclo*hexanone yielded pure 2-iodo-4-nitro-1-*n*-octyloxybenzene (54%), m. p. and mixed m. p. with specimen from nitration 50—51°, after four crystallisations from light petroleum.

3-*Iodo*-4-n-*octyloxyaniline*.—An alcoholic solution of the nitro-compound was reduced in the usual way with stannous chloride and concentrated hydrochloric acid. The solution was reduced to half its volume by distillation and the residue neutralised carefully with 10N-sodium hydroxide at 0—10°. The amine extract with chloroform was washed with water and dried. Removal of the solvent and distillation under reduced pressure gave 3-*iodo*-4-n-*octyloxyaniline* (Found: I, 36·3. $C_{14}H_{22}ONI$ requires I, 36·6%) as a pale yellow viscous oil, b. p. 174—178°/1 mm., in 58% yield. The *acetyl derivative* was prepared by use of acetic anhydride and ice-cold 2N-sodium hydroxide. The crude product was crystallised from methanol and then from benzene–light petroleum (1 : 1·5 by volume), after which the m. p. was 122—122·5° (Found: C, 49·4; H, 6·0; N, 3·2; I, 32·2. $C_{16}H_{24}O_3NI$ requires C, 49·35; H, 6·2; N, 3·6; I, 32·6%).

o-*Fluorophenol*.—*o*-Fluoroanisole [9] (113 g.) was refluxed for 14 hr. in glacial acetic acid (220 ml.) and 48% hydrobromic acid (220 ml.). Solid sodium hydrogen carbonate was added to the cooled reaction mixture whereupon, before reaching neutral point, the phenol separated as an oily upper layer. The oil was stirred with solid sodium hydrogen carbonate until no more carbon dioxide was evolved, then chloroform was added, and the organic layer removed and dried (Na_2SO_4). The solvent was removed and *o*-fluorophenol, 56 g. (56%), b. p. 142—148°, obtained by distillation of the residue through a short fractionating column.

1-*Fluoro*-2-n-*octyloxybenzene*.—*o*-Fluorophenol was octylated as for *o*-iodophenol. The *octyl ether*, a pale yellow oil, b. p. 156—160°/20 mm., was obtained in 75% yield (Found: C, 74·8; H, 9·3. $C_{14}H_{21}OF$ requires C, 75; H, 9·4%).

2-*Fluoro*-4- *and* -6-*nitro*-1-n-*octyloxybenzene*.—The nitration conditions were as for the iodo-analogue. The addition time was 40 min., stirring was continued for a further 20 min., and the mixture remained homogeneous. The oily nitration product (after dilution) was extracted with ether, and the extract washed (aqueous sodium carbonate and water) and dried (Na_2SO_4). The ether was removed and the residue distilled under vacuum. The mixture (80%) of 4- and -6-*nitro-isomers* (Found: N, 5·14. Calc. for $C_{14}H_{20}O_3NF$: N, 5·4%), b. p. 140—160°/0·1 mm., was collected. Attempts to separate the isomers by crystallisation were unsuccessful and the mixture was reduced and acetylated.

3-*Fluoro*-4-n-*octyloxyacetanilide*.—The mixture of 2-fluoro-4- and -6-nitro-1-*n*-octyloxybenzenes was reduced as for the 2-iodo-4-nitro-analogue. It was not possible to separate the isomeric amines by distillation, and these were obtained as a wax (55%), b. p. 140—150°/0·5 mm., which could not be crystallised. Acetylation of the amines with acetic anhydride and

[7] Hodgson and Moore, *J.*, 1925, 2260.
[8] Gray and Jones, *J.*, 1954, 1467.

ice-cold 2N-sodium hydroxide gave a solid, m. p. 69—74°, which crystallised readily from aqueous alcohol. Two further crystallisations from benzene–light petroleum (1 : 1 v/v) gave colourless needles of 3-*fluoro*-4-n-*octyloxyacetanilide* (53%), m. p. 83·5—84·5° (Found: C, 68·5; H, 8·6; N, 5·3. $C_{16}H_{24}O_2NF$ requires C, 68·3; H, 8·5; N, 5·0%). The isomeric acetylamine was not isolated, but the orientation of the substituents in the product was proved by the following small-scale experiments.

2-Fluoro-4-nitrophenol [9] (3 g.) was octylated (cf. above alkylation of 2-iodo-4-nitrophenol), and the crude, oily product reduced and acetylated as for the analogous iodo-derivative. The resulting 3-fluoro-4-*n*-octyloxyacetanilide was purified and had m. p. 83—84°, undepressed on admixture with the above product.

3′-*Fluoro- and* 3′-*Iodo*-4′-n-*octyloxydiphenyl*-4-*carboxylic Acids*.—The preparations were carried out with the pure 3-fluoro- and 3-iodo-4-octyloxyacetanilides. The purified acetylamine (20 g.) was dissolved in a mixture of glacial acetic acid (140 ml.) and acetic anhydride (60 ml.) and placed in a bolt-head flask fitted with an efficient stirrer, a thermometer, and a dropping funnel. Fused sodium acetate (anhydrous) (20 g.) was finely powdered and added to the solution, together with phosphoric oxide (2 g.). The mixture was stirred and cooled in ice, and the temperature maintained at 8° during the gradual addition of nitrosyl chloride [10] (20 g.) in glacial acetic acid (20 ml.) and acetic anhydride (10 ml.), and for 30 min. after the addition. The mixture was poured into ice and water (1000 g.) and stirred to hydrolyse the acetic anhydride. The suspension of the greenish-yellow, oily *N*-nitroso-derivative was extracted with methyl benzoate (500 ml.) which was then washed first with water and then with 2N-aqueous sodium hydroxide (400 ml.), and dried (Na_2SO_4) for a few minutes. The dried extract was then stirred for 60 hr. with anhydrous sodium sulphate (48 g.) and sodium carbonate (32 g.), whereupon the salts were filtered off and the methyl benzoate distilled off under vacuum. Distillation of the residues gave the following fractions: Fluoro-; 195—205°/0·1 mm. (5 g.), 205—212°/0·1 mm. (4·5 g.), 212—230°/0·1 mm. (4·5 g.); Iodo-; 190—220°/0·1 mm. (2·6 g.), 220—235°/0·1 mm. (5·6 g.), 235—242°/0·1 mm. (0·4 g.). These oily fractions, consisting of mixtures of the methyl 3′-fluoro- and 3′-iodo-4′-octyloxydiphenyl-2-, -3-, and -4-carboxylates, were hydrolysed separately by boiling for 90 min. with 80% methyl alcohol (25 ml.) containing 2·5 g. of potassium hydroxide, for each 1 g. of oil. The hydrolysates were diluted with water and acidified with concentrated hydrochloric acid to precipitate the gummy mixture of acids. Although the fractions were hydrolysed separately, crystallisation of the gums from glacial acetic acid gave separation of the 4-carboxylic acid from each fraction. This applied to both fluoro- and iodo-derivatives, and the yield of the 4-carboxylic acid increased with the b. p. of the fraction hydrolysed. The separate fractions of the 4-carboxylic acids were combined and crystallised to constant m. p. from benzene and glacial acetic acid. Both acids were obtained as colourless needles and exhibited mesomorphism (see Table 1 for transition temperatures): 3′-*iodo*-4′-n-*octyloxydiphenyl*-4-*carboxylic acid*, 2·2 g. (9·5%) (Found: C, 55·3; H, 5·2; I, 28·6. $C_{21}H_{25}O_3I$ requires C, 55·75; H, 5·5; I, 28·1%) had m. p. 180·5°, and 3′-*fluoro*-4′-n-*octyloxydiphenyl*-4-*carboxylic acid*, 2·5 g. (10·3%) (Found: C, 73·0; H, 7·3. $C_{21}H_{25}O_3F$ requires C, 73·2; H, 7·3%), had m. p. 119·5°.

Because of their mesomorphic behaviour, the orientation in these acids was obviously such that the carboxyl group was in the 4-position in the diphenyl ring, but it was decided to verify this chemically. Each acid (0·5 g.) was boiled for 1 hr. with glacial acetic acid containing excess of potassium permanganate. The mixtures were cooled and the manganese dioxide was filtered off and extracted several times by stirring with aqueous ammonium hydroxide. Acidification of the ammoniacal filtrates gave a precipitate of terephthalic acid, confirmed by conversion into dimethyl terephthalate, m. p. 140°.

n-*Propyl* 3′-*Fluoro*-4′-n-*octyloxydiphenyl*-4-*carboxylate*.—The *ester* was prepared in the usual way from the acid, propan-1-ol, and concentrated sulphuric acid, and crystallised from methyl alcohol and from light petroleum. The colourless mesomorphic product had m. p. 46° (Found: C, 74·6; H, 8·1. $C_{24}H_{31}O_3F$ requires C, 74·6; H, 8·0%).

We thank the Distillers Co. Ltd. and Imperial Chemical Industries Limited for grants to the Department.

THE UNIVERSITY, HULL. [*Received, December 17th*, 1958.]

[9] Berg and Newbery, *J.*, 1949, 642.
[10] " Organic Reactions," John Wiley and Sons, Inc., New York, Volume II, p. 251.

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299. *The Intensity of Ultraviolet Light Absorption by Monocrystals. Part III.*[1] *Absorption by Anthracene at* 295° K, 90° K, *and* 4° K *of Plane-polarised Light of Wavelengths* 1600—2750 Å.

By L. E. Lyons and G. C. Morris.

Quantitative measurements of the absorption by anthracene monocrystals of plane-polarised light are reported from 1600 to 2750 Å at 4° K, 90° K, and 295° K. Five transitions are detected and these are discussed in terms of the excited electronic states of the anthracene molecule. The Davydov splitting of the molecular transition at 4·8 ev is confirmed by the measurement of the component polarised perpendicularly to the *b* crystal axis. The various upper states are assigned to symmetry species.

The interpretation of the spectrum [1] of the anthracene molecule has been greatly assisted by the study of crystal spectra with plane-polarised light. In the past, experimental difficulties have limited observations of intensity of absorption to the region below 48,000 cm.$^{-1}$. Although there have been one or two observations [2] of aromatic crystal spectra in the vacuum region with polarised light no work has been reported on anthracene except for a brief mention [3] of a qualitative experiment. No previous work at low temperatures with polarised radiation in the vacuum region is known to us. The region above 48,000 cm.$^{-1}$ is important to the understanding of the anthracene spectrum in several respects. One object of the present work was to test the prediction of the crystal splitting of the second main absorption system, found in solution near 40,000 cm.$^{-1}$. In Part II it was found that the *b* component of this transition had an extinction coefficient which agreed with the value predicted. The *a* component (polarised perpendicularly to the *b* crystal axis) could not be found below 46,000 cm.$^{-1}$ and was expected to lie at higher energies with a calculated molar extinction coefficient of 170,000, the molecular transition being polarised along the longer in-plane axis.

Experimental

Anthracene was chromatographed [cf. ref. 4]. Crystals were prepared by sublimation in carbon dioxide in the dark, transferred to polished fluorite or lithium fluoride discs and an appropriate section selected. Axes were determined by conoscopic investigation under a Zeiss polarising microscope, thicknesses being determined by use of an Ehringhaus compensator. The birefringence at 5461 Å was taken as 0·134.[5] The crystal holder allowed rotation of the crystal through known angles, as well as lateral and vertical movements. The light source was an Allen hydrogen arc [6] with a fluorite window attached by an O-ring seal to the metal casing and operated usually at 4 A, 60 V. Calibration arcs were a standard copper arc in a nitrogen stream, or a copper hollow-cathode tube with a sapphire window.

The light was condensed by a lithium fluoride lens on the crystal of which the requisite area was left unmasked. The emergent light was condensed to a beam about 1 mm. in diameter at the slit. The beam was analysed by a special Wollaston prism designed to fit inside the spectrograph and produce at the plate two beams polarised mutually perpendicularly about 1 mm. apart. With all optical components and crystals about 0·1 μ thick examination was possible to about 64,000 cm.$^{-1}$. The prism itself transmitted to about 67,000 cm.$^{-1}$. Crystals thicker than 0·3 μ were too thick for measurement above 50,000 cm.$^{-1}$.

The low-temperature runs were done in either a helium cryostat [7] fitted with fluorite windows

[1] Part II, Bree and Lyons, *J.*, 1956, 2662; see also Craig, Hobbins, and Walsh, *J. Chem. Phys.*, 1954, **22**, 1616; Craig and Hobbins, *J.*, 1955, 539 and 2309; Sidman, *Phys. Rev.*, 1956, **102**, 96; Ferguson and Schneider, *J. Chem. Phys.*, 1958, **28**, 761; Perkampus, *Z. phys. Chem.* (*Frankfurt*), 1957, **13**, 278.
[2] Nelson and Simpson, *J. Chem. Phys.*, 1955, **6**, 1146; Romand and Vodar, *Compt. rend.*, 1951, **233**, 930.
[3] Dunn and Lyons, quoted by Lyons, *J. Chem. Phys.*, 1955, **23**, 1973.
[4] Lyons and Morris, *J.*, 1957, 3648.
[5] Obreimov, Prikhotjko, and Rodnikova, *Zhur. eksp. teor. Fiz.*, 1948, **18**, 409.
[6] Allen, *J. Opt. Soc. Amer.*, 1941, **31**, 268.
[7] Walsh, Ph.D. Thesis, Sydney, 1958.

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or else a conventional low-temperature apparatus. Oxygen was removed from the light path by blowing a continuous oxygen- and water-free stream of nitrogen between the components. A fluorite window covered the slit.

The Hilger 3 metre normal incidence vacuum grating spectrograph was used in the 1st order (5·78 Å/mm. dispersion) and operated at a pressure of 10^{-4} mm. Hg or less, vapours being trapped by liquid-air containers. Ilford Q_1 and Q_2 plates were developed in Ilford Developer 19b for 3 min. Ten exposures could be placed on a plate, comparison spectra being obtained by means of a diaphragm before the plate. Each wavelength setting gave a span of 1400 Å on the plate. Blackening was measured on a Hilger recording microphotometer, each spectrum being traced twice. The calibration arc was traced and then the spectrum to be measured, part of

FIG. 1. *Absorption spectra of anthracene.* . . . . *solution in* n*-heptane;* —— *b crystal spectrum with the electric vector of the light parallel to b crystal axis;* — · — · — *a crystal spectrum electric vector perpendicular to b in* (001) *plane.*

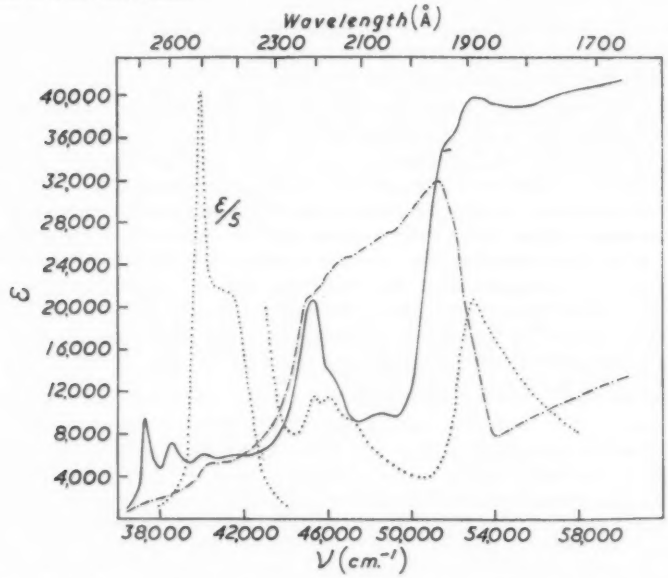

TABLE 1. *Extinction coefficients,* $\varepsilon = (1/cd)\log_{10}(I_0/I)$ *at turning points; room temperature.*

c, lowest wave-length observed with continuum.
l, observed with line source. s, shoulder.
* Maximum.

λ (Å)	ν (cm.⁻¹)	ε_b	λ (Å)	ν (cm.⁻¹)	ε_a
2680·5 *	37,315 *	9600			
2638	37,910	5000			
2595 *	38,530 *	7200			
2546	39,280	5400			
2490 *	40,160 *	6200	2500 s	40,000 s	5000
			2220 s	45,050 s	21,000
2210 *	45,250 *	20,800			
2170 s	46,080 s	14,000	2130 s	46,950 s	25,000
2110	47,390	9200			
2070 *	48,310 *	10,400	2050 s	48,780 s	27,200
2032	49,200	9600			
1930 s	51,810 s	36,000	1950 *	51,280 *	32,000
1890 *	52,910 *	40,000			
			1850	54,050	8000
1667 c	60,000 c	41,500	1667 c	60,000 c	13,400
1660 l	62,500 l	42,000	1600 l	62,500 l	15,000

the calibration arc being also traced at both ends of this spectrum. Exact superposition of corresponding arc lines at either end of the tracings was always possible. Wavelengths reduced to vacuum were calculated from the tracings. For photoelectric measurement, a 1P28 photomultiplier coated with sodium salicylate [8] was fitted inside the spectrograph, one or other polarised beam being cut off by a movable diaphragm. One of four pre-set slits mounted

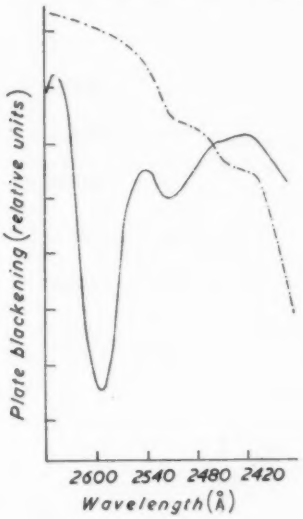

FIG. 2. *Microphotometer traces of b and a crystal spectra at 90° K.*

———— *electric vector parallel to b.*

—·—·— *a.*

TABLE 2. *Reduced oscillator strengths* ($f_{a,b} = 1{\cdot}44 \times 10^{-9} \int \varepsilon_{a,b}\, d\nu$) *in the crystal at room temperature.*

(abs., absorption spectrum; ref., reflection spectrum; r.i. refractive index); * Present work.

System	Range of ν (cm.$^{-1}$)	f_b	f_a	Method
I		0·033(?)	0·015	abs.[a]
		0·06	0·013	ref.[a]
	25,000—33,000	0·064	0·025	abs.[b]
		0·10	0·057	r.i.[c]
		0·057	0·013	r.i.[d]
		0·04	0·017	abs.[e]
II	37,000—41,000	0·047		abs.[b]
	37,000—41,000	0·035	(0·020)	abs.*
	41,000—54,000		0·368	abs.*
III		0·16		ref.[f]
		0·4		ref.[b]
		0·09		abs.[f]
	41,000—47,500	0·099		abs.*
IV	47,500—49,500	0·029		abs.*
V	49,500—60,000	$\geqslant$0·55		abs.*
	54,000—60,000		0·094	abs.*

[a] Borisov, *Trudy Inst. Fiz. Akad. Nauk Ukrain. S.S.R.*, 1953, 102. (See Technical Translation TT-613, 1956, Nat. Res. Council, Canada.) [b] Part II. [c] Ref. 5. [d] Eichis, *Z. exsp. teoret. Fiz.*, 1950, **20**, 471. [e] Brodin and Prikhotjko, *Optika i Spectroskopiya*, 1957, **2**, 448; Kharitonova, *ibid.*, 1958, **5**, 29. [f] Ref. 19.

on the plate holder could be selected. The incident and transmitted beams were examined alternatively in each polarisation, similarly polarised beams always falling on the same area to avoid errors.[9] For the low-temperature work, the incident beam was examined after the

[8] Williams, Meharry, Maslen, and Falconer, *J. Opt. Soc. Amer.*, 1954, **44**, 654; Bolton and Williams, *Nature*, 1952, **169**, 325; *Brit. J. Appl. Phys.*, 1954, **4**, 6; Johnson, Watanabe, and Tousey, *J. Opt. Soc. Amer.*, 1951, **41**, 702.

[9] Norman and Kay, *J. Sci. Instr.*, 1952, **29**, 33; Clancy, *J. Opt. Soc. Amer.*, 1952, **42**, 357.

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transmitted beam spectrum was obtained. The photomultipler response (assumed directly proportional [10] to the light flux) was measured on an Electronic Industries Ltd. Vibron electrometer model 33B. The wavelength setting calibrated by a mercury lamp could be altered by rotating the grating and plate holder around the Rowland circle by means of an external handle.

FIG. 3*a*.

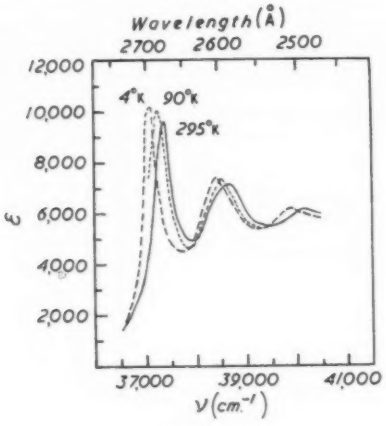

FIG. 3*b*.

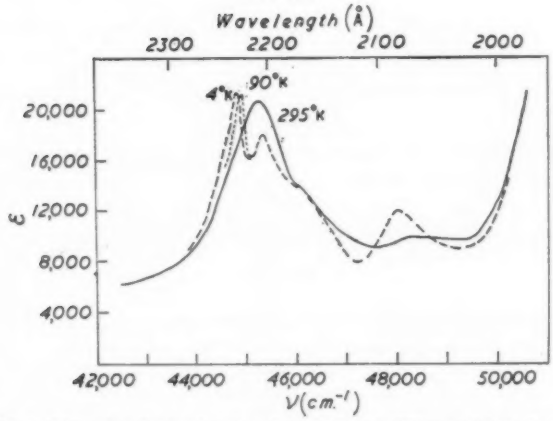

FIG. 3. *Effect of lowering the temperature from* 295° K *to* 90° K *and* 4° K (*b polarisation*).
(*a*) 37,000 cm.$^{-1}$ region; (*b*) 46,000 cm.$^{-1}$ region.

Molar extinction coefficients were obtained by both photographic photometry and photoelectric methods. For the former, light filters of nickel gauze,[11] neutral as calibrated on a Uvispek spectrophotometer to 45,500 cm.$^{-1}$, were assumed neutral to 62,500 cm.$^{-1}$. This assumption was later proved correct by photomultiplier measurement of their optical density. Eight filters of optical densities from 0·16 to 1·14 were used. Failure of the reciprocity law was negligible over the range of times considered (less than six-fold). Exposure times varied between 1 min. and 1½ hr. It was preferable to cut down exposure time by opening the slit to as much as a 3 Å band-pass (after ascertaining that no fine structure was present) in order to reduce the effect of stray light which rendered the photometry above 55,500 cm.$^{-1}$ difficult.

[10] Engstrom, *J. Opt. Soc. Amer.*, 1947, **37**, 420.
[11] Sawyer and Vincent, *J. Opt. Soc. Amer.*, 1943, **33**, 247.

The photomultiplier method was the more accurate for extinction coefficients, but the signal : noise ratio was too small for high accuracy above 55,000 cm.$^{-1}$. Wavelength measurements were best done photographically. The lamp, provided it was vacuum-tight, needed no stabilisation for reproducibility.

The solution spectrum was obtained in 1 mm. " Ultrasil " cells with *n*-hexane as solvent on both the vacuum instrument and a " Spectracord " double-beam recording spectrophotometer.

The results are shown in Figs. 1—3 and Tables 1—5. The errors in wavelengths depend on the band shape, sharper bands being accurate to 2 Å. The errors in extinction coefficient were about 15% (<50,000 cm.$^{-1}$) or 30% (>50,000 cm.$^{-1}$) with the photographic method, but about 10% and 20% with the photomultipler; the main error lay in the measurement of the crystal thicknesses. Errors in oscillator strengths arise mainly from determining the exact wavenumber spread of the transition but, with $\Delta\nu$ as stated in the Tables, the errors in f correspond to those in ε. A further error may arise from surface effects.[12] Whilst these may alter the bulk spectrum to a certain extent, no evidence of this was seen.

The " reduced " oscillator strength is convenient in the consideration of crystal transitions and may be defined so that $f_a + f_b + f_p$ approximates to f for a solution. The Russian workers calculate oscillator strengths for the crystal which are three times as great as f_a or f_b, so their results have been divided by three in Table 2.

TABLE 3. *Oscillator strengths,* $f = 4{\cdot}31 \times 10^{-9} \int \varepsilon \, d\nu$.

	I	II	III	V
Vapour	0·11 [a]; 0·02 [b]	0·93 [b]		
Solution	0·10 [c]	1·56 [b]; 1·9 [c]; 2·3 [d] 1·6 [e]	⩽0·28 [d]; 0·22 [e] 0·21 [e]	0·6 [d]; 0·5 [e] 0·41 [e]

[a] Brodin and Prikhotjko, *Optika i Spectroskopiya*, 1957, **2**, 448; Kharitonova, *ibid.*, 1958, **5**, 29. [b] Ferguson and Schneider, *Canad. J. Chem.*, 1957, **35**, 1117. [c] Calc. from " Catalog of Ultraviolet Spectrograms," Amer. Petroleum Inst., Project 44 at Nat. Bur. Stand., Nos. 91 and 170. [d] Klevens and Platt, *J. Chem. Phys.*, 1949, **17**, 470. [e] Ref. 21. [e] Present work.

Discussion

We now attempt to explain the main features of the observed spectrum in terms of π–π transitions. Only the theoretically expected singlet upper states are considered. It must be realised that triplet $2p\pi$ states and other states expected in the crystal such as ionised states and states involving atomic orbitals with $n \geqslant 3$ may possibly occur in this spectral region. A feature of the crystal spectrum is that there are no Rydberg bands clearly visible in the region in which they occur in the vapour. This agrees with the theory that such bands in the vapour are removed to much lower energies in the crystal. The ionisation and the photoelectric properties of the crystal in this region will be discussed in a subsequent paper.

The group-theory notation is that recommended [13] in 1955 and differs from that used in Part II. Throughout the discussion " *a* " refers to a direction perpendicular to the *b* crystal axis and lying in the (001) plane.

System I has been studied previously by a number of workers whose results are included for comparison. Table 2 shows that even for this most accessible system there is a large variation in the experimentally determined oscillator strengths. Nonetheless, there is clear confirmation of the *z* (short molecular axis) polarisation of the transition and of the $^1L_a : B_{1u}^+$ nature of the excited electronic state. Here Platt's symbol precedes the result calculated by Pariser.[14]

From the results for crystal and solution it follows that Obreimov, Prikhotjko, and Rodnikova's [5] f values for the crystal are high. Calculation of $f_p = 0{\cdot}01$ by the difference between $f_a + f_p$ and $f_{soln.}$ agrees with the value calculated by first-order theory which

[12] Ferguson and Schneider, *J. Chem. Phys.*, 1958, **28**, 761.
[13] Mulliken, *J. Chem. Phys.*, 1955, **23**, 1997.
[14] Pariser, *J. Chem. Phys.*, 1956, **24**, 250.

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gives $f_p' = 0{\cdot}01$ (see Part II). The transition to the low-lying ^1L_b : $^1B_{2u}^-$ state is expected by Pariser and by Ham and Rudenberg [15] to be weak and to be buried beneath System I.

System II was observed in *b* polarisation both earlier (Part II) and in the present work which gives a slightly lower value for f_b but about the same value for ε_b. The general discussion of Part II is confirmed, as is the assignment of the polarisation as *y* (long molecular axis). The earlier work, however, could not investigate the *a* polarised absorption expected (on the basis of the reflection spectra taken at less than 45,000 cm.$^{-1}$) to appear between 52,000 and 66,000 cm.$^{-1}$ with a predicted f_a of 0·5. In the present work strong absorption was found to extend over the interval 41,000—54,000 cm.$^{-1}$ with an observed f_a of 0·37. This absorption is therefore taken to arise chiefly from System II of the molecular spectrum. There could be some absorption arising from other molecular systems. For example the *a* components of Systems III and IV are both likely to appear in this region. Both components of System II have now been measured in the crystal and the earlier result [3] is confirmed and made quantitative. The observed spectrum therefore confirms the theory [16] of the Davydov splitting of System II. The upper state of System II is identified as ^1B_b by Platt [17] and by Ham and Rudenberg. Pariser identifies the upper state of the very strong transition as $^1B_{2u}^+$. Both assignments are consistent with the observed spectrum.

System II has $f = 1{\cdot}6$ in solution but $f_a + f_b = 0{\cdot}43$ only. This reduction in intensity is expected for a transition polarised along the longer molecular axis. The values calculated by first-order theory are $f_a' = 0{\cdot}48$ and $f_b' = 0{\cdot}04$. Consideration of intensity therefore confirms the polarisation of the transition deduced previously and also shows that the major factor causing the apparent great reduction in intensity on going from solution to crystal is simply the geometry of the molecular arrangement. The peculiar shape of the *a* component of II seems likely to be due to the presence of three close-lying *a* components from systems II, III, and IV. Three such upper states must mix greatly with each other in the crystal. There is predicted a further transition near system II which marks a $^1B_{1u}^+$ level according to Pariser and a second ^1L_a state according to Ham and Rudenberg. In both cases the molecular polarisation would be short-axis. In both Part II and the present work there was observed a weak extra absorption (system II′) at 40,000 cm.$^{-1}$.

At low temperatures a vibrational interval of about 980 cm.$^{-1}$ appeared in the *a* polarisation (Fig. 2). System II′, although possibly due to disoriented molecules, could conceivably mark a level expected by theory. Previously the B_{3g} level predicted by Coulson [18] was regarded as possibly present. The more recent theories make alternative assignments more likely than B_{3g}. Platt's original symbolism allowed for only one state of type ^1L_a. Ham and Rudenberg make no calculations for the second ^1L_a state but use the symbolism to indicate the empirical similarity between a pair of levels over a range of compounds.

System III was measured in Part II in *b* polarisation both by absorption ($f_b = 0{\cdot}09$) and reflection ($f_b = 0{\cdot}16$). The result deduced in Part II for f_b, also based on reflection measurements, was $f_b = 0{\cdot}43$. (In the summary of Part II the value is given incorrectly.) Bree's result [19] of 0·16 was based on later and fuller work than that reported in Part II and we consider it the more reliable of the two reflection results. In the present work f_b was found to be 0·10. Therefore the conclusion of Part II is confirmed and System III marks a *z* polarised molecular transition. If this transition marks Platt's ^1C_b state then it is electronically forbidden in the free molecule. The observed intensity is then to be explained by intra- and/or inter-molecular stealing from neighbouring bands of similar crystal symmetry. Ham and Rudenberg differ from Platt and assign the upper state as

[15] Ham and Rudenberg, *J. Chem. Phys.*, 1956, **25**, 1.
[16] Craig, *J.*, 1955, 2302.
[17] Platt, *J. Chem. Phys.*, 1949, **17**, 481.
[18] Coulson, *Proc. Roy. Soc.*, 1948, **60**, 257.
[19] Bree, Ph.D. Thesis, Sydney, 1958.

^1B_a. This agrees with the observed polarisation, but Platt's assignment cannot be ruled out on these grounds. The consideration of f_b values (calculated as 0·005 for long-axis polarisation and 0·2 for for short-axis) confirms the short-axis assignment especially when it is remembered that the f value for the solution is likely to be high owing to the overlap with the next transition. Because ε_a was greater than ε_b in this region Craig [20] came to the opposite conclusion about this polarisation. At that time however Craig had not proposed the theory of the Davydov splitting of System II and so did not associate the larger a absorption with System II. The predicted splitting of 16,000 cm.$^{-1}$ compares with the present observed splitting of 8000—15,000 cm.$^{-1}$ (Fig. 1). The short-axis polarisation now confirmed agrees with Pariser's identification of the upper state as $B_{1u}{}^+$ although both his calculated energy and oscillator strength are higher than those observed. The Davydov splitting expected for System III is likely to be very much less than for System II and therefore the previous agreement is unlikely to be upset by such considerations. Nor could intensity stealing by an intermolecular mechanism in the crystal (which would have increased the a absorption more than the b) have reversed the polarisation.

System IV has not previously been discussed either in solution or in crystal and here was observed definitely only in b polarisation. It is weak ($f_b = 0{\cdot}029$). It is not a " hot " band associated with the strong b transition at 50,000 cm.$^{-1}$ since it appears even more definitely at 90° K and at 4° K (Fig. 3). The corresponding a component could well be buried beneath the strong a absorption at similar frequencies. In the solution spectrum [21] there is no region of absorption near 48,000 cm.$^{-1}$ which clearly marks a separate electronic transition. In phenanthrene, however, an " extra " band is probably present. Pariser predicts a $^1B_{2u}{}^+$ level at 7·2 ev, a transition to which is of appropriate intensity and is long-axis polarised. Ham and Rudenberg's second ^1L_b state is also a possibility in this instance in view of the fact that System V, which they assigned as the second ^1L_b, has the wrong polarisation property. Because of the lack of clear observation of the a component it is impossible to conclude what is the polarisation of System IV, especially as intermolecular intensity stealing from System V could well have augmented the f_b value of IV. There is no argument against the $^1B_{2u}{}^+$ assignment.

System V is intense in solution ($f = 0{\cdot}4$) and presumably a large amount of the crystal absorption in b polarisation between 50,000 and 60,000 cm.$^{-1}$ is derived from this molecular system. If this is so then the fact that f_b is comparable with $f_{\text{soln.}}$ indicates that the transition is z polarised. The corresponding a absorption between 54,000 and 60,000 cm.$^{-1}$ and beyond may correspond wholly or in part to the b component between 50,000 and 60,000 cm.$^{-1}$. The value of f_a is in this case again in fair agreement with that expected for a z-polarised molecular transition. In this region, however, crystal effects are likely to be relatively more important than at lower energies. The interpretation of the crystal spectrum in terms of molecular properties must therefore be made with reservations.

The effect on the spectrum of lowering the temperature to 90° K and to 4° K was examined. Results were as follow: (i) In System II the b-polarised peaks became sharper and moved to lower energies (see Table 4 and Fig. 3); the extinction coefficients at the peaks became greater. (ii) In System II the b-polarised peak split into two with a separation of 630 cm.$^{-1}$ at 4° K. This presumably indicates a totally symmetric vibration in the third $B_{1u}{}^+$ excited state. (iii) In a polarisation shoulders appeared at 39,950, 40,900, 43,977, 46,080, 48,080, 48,780, 49,260, 49,580, and 49,930 cm.$^{-1}$. (iv) The peak in System IV was sharpened, increased in height, and moved to slightly lower energies.

The general lack of structure in the anthracene spectrum compared, for example, with that [7] in the naphthalene band at 32,000 cm.$^{-1}$ continues in the vacuum region. This diffuseness is attributable to the influence of lattice vibrations [22] and any mixing of the upper levels with conduction levels.

[20] Craig, *Rev. Pure Appl. Chem.* (*Australia*), 1953, **4**, 207.
[21] Jones and Taylor, *Analyt. Chem.*, 1955, **27**, 228.
[22] Moffitt, personal communication.

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TABLE 4. *Variation in positions of band maxima (cm.$^{-1}$) with temperature.*

T (°K) = 295	37,320	38,530		45,250	46,080	48,310
90	37,210	38,510	44,840	45,290	46,080	48,080
4	37,110	38,420	44,700	45,330	46,020	48,010

On the whole lowering the temperature added little new knowledge of the spectrum beyond establishing that the ground state of System IV was not vibronic.

TABLE 5. *Some electronic states of anthracene observed and calculated.*

	Obs. in solution		Obs. in crystal			Platt [a]			Ham and Rudenberg [b]		Moffitt [c]	Pariser [d]		
							Assign-		Assign-	Calc.	Calc.	Assign-	Calc.	
	ev	f	ev	f_a	f_b	pol.	ment		ment	ev	f	ment	ev	f
I	3·4	0·1	3·1	0·02	0·06	z	z	^1L_a	z ^1L_a	3·6	0·11	z B_{1u}^-	3·6	0·4
							y	^1L_b	y ^1L_b	3·2	0·0005	y B_{2u}^-		
II	4·8	1·6	4·6, 5·7	0·4	0·04	y	y	^1B_b	y ^1B_b	5·2	1·45 >	y B_{2u}^+	5·5	3·2
									z ^1L_a			z B_{1u}^+	5·25	0·1
II′			5·0	0·01		?								
III	5·6	0·2	5·5		0·1	z	forb.	^1C_b	z ^1B_a	5·4		z B_{1u}^+	6·6	0·6
IV			6·0		0·03	?						y B_{2u}^+	7·2	0·1
V	6·7	0·4	6·3	⩾0·1	⩾0·6	z	z	^1B_a	y ^1L_b			z B_{1u}^+	7·8	

[a] Ref. 17. [b] Ref. 15. [c] Moffitt, *J. Chem. Phys.*, 1954, **22**, 320. [d] Ref. 14.

Table 5 summarises the experimental and theoretical conclusions.

We thank General Motors Holden Ltd. for a scholarship (to G. C. M.) and grant; Mr. J. W. White for aid in the use of the helium cryostat; Dr. A. L. G. Rees of C.S.I.R.O. for the loan of the hollow-cathode tube; Mr. N. Whittem of the Australian Atomic Energy Commission for the use of the microphotometer.

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300. *Overcrowding Distortions in Aromatic Molecules and Crystals.*

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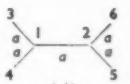
Calculation of the loss of resonance energy (called deformation energy) due to steric deformation in the three overcrowded molecules, 3 : 4-5 : 6-dibenzophenanthrene, 5 : 6-7 : 8-dibenzoperylene, and 1 : 12-5 : 6-7 : 8-tribenzoperylene, shows that the large size and more rigid character of the polynuclear framework exerts hardly any influence on the strain energy. It is suggested, on the basis of similar calculations, that in tetrabenzoperopyrene, where there are two overcrowded regions, the molecule takes up a propeller-like shape. An estimate is made of the deformation energy per molecule in the molecular crystals of chrysene and 20-methylcholanthrene, where accurate X-ray analysis by Iball shows that the molecules are deformed out of a plane. The energies turn out to be very small. ~50 cal., *viz.*, per mole.

COULSON and SENENT [1] have developed a simple potential function for the out-of-plane displacements of ethylenic and aromatic molecules. This involves the use of only two force constants. It has been applied with success to account for the out-of-plane frequencies of ethylene and benzene, and of molecules as complex as naphthalene. A further application [2] of this potential function was to the calculation of out-of-plane displacements and energy of overcrowding in 3 : 4-5 : 6-dibenzophenanthrene (I) where

[1] Coulson and Senent, *J.*, 1955, 1813.
[2] *Idem*, *J.*, 1955, 1819.

both theory and experiment showed that the overcrowding was relieved almost wholly by displacements of the various carbon and hydrogen atoms in a direction normal to the mean plane of the molecule. In the present study we make use of the Coulson–Senent potential function (hereafter referred to as C.S.) in three ways. In the first we consider the displacements and overcrowding energy in a series of polynuclear hydrocarbons (I—III), of which the first is that already dealt with by Coulson and Senent. The purpose of these calculations is to discover the extent to which the molecular deformations depend on additional structure and rigidity in the carbon framework. Our second problem concerns the prediction of the configuration of the recently reported tetrabenzoperopyrene [3] (IV) where there are two regions of overcrowding, and two main alternative ways exist whereby this can be relieved. Finally we make use of the C.S. potential function to discuss certain polynuclear hydrocarbons, notably chrysene and 20-methylcholanthrene, where recent accurate *X*-ray analysis has shown that the molecules are distorted in the solid phase, presumably as a result of intermolecular forces.

Force-field and Method of Calculation.—We assume, as in the pioneer work of Coulson and Senent, that in all these molecules the relief of overcrowding takes place by displacements of atoms perpendicular to the undistorted molecular plane. All other changes in the molecular shape, such as bond lengths and interbond angles, are supposed to be negligible. Then the potential energy V is a function only of the atomic displacements $z_1 \ldots$ so that $V = V(z_1, \ldots)$. We presume that the equilibrium values of the z_r are such as to minimise V. For the explicit expression of V, we use the C.S. function. This is the sum of a set of terms, one for every carbon atom around which the three bond directions are not coplanar ("lack-of-planarity" term), and one for each carbon–carbon bond around which there is any degree of torsion ("torsion" term). These terms may all be found from a generalisation of the formulæ given in ref. 1, and appropriate to a situation in which all five bond lengths (see *A*) are equal. There it was shown that the lack-of-planarity term at carbon $C_{(1)}$ is



(*A*)

Part of a condensed polynuclear hydrocarbon.

$$\tfrac{1}{2}k_1(z_2 + z_3 + z_4 - 3z_1)^2$$

and the torsion term around $C_{(1)}$–$C_{(2)}$ is

$$\tfrac{1}{2}k_2(z_3 - z_4 + z_5 - z_6)^2$$

If some or all of the four bond lengths such as $C_{(1)}$–$C_{(3)}$ are different from a, these formulæ need modification. All such modifications are included in the following rule. If a bond such as $C_{(1)}$–$C_{(3)}$ has its length b then, in these two formulæ, z_3 must be replaced by

$$z_1 + \frac{a}{b}(z_3 - z_1)$$

If more than one such bond is altered, all the corresponding changes in the z_r must be made. When this has been done, $V(z_1 \ldots)$ is merely the sum of the necessary total of planarity and torsion terms. In the cases of (I, II, III), for example, there are 22, 28, and 30 planarity terms, and 26, 34, and 37 torsion terms respectively. In our calculations the numerical values adopted are those chosen by Coulson and Senent [1] from a study of vibrational frequencies:

$$a = \text{C–C} = 1{\cdot}40 \text{ Å}; \; b = \text{C–H} = 1{\cdot}08 \text{ Å}$$

$$k = 0{\cdot}1474 \times 10^5 \text{ dynes cm.}^{-1}; \; k_2 = 0{\cdot}0553 \times 10^5 \text{ dynes cm.}^{-1}.$$

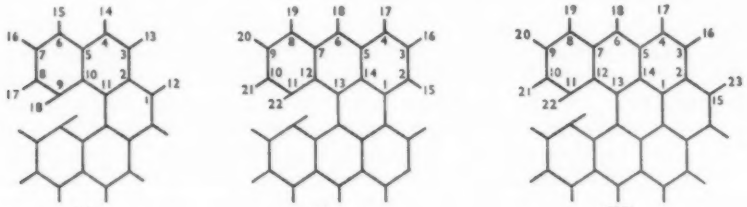
Of (I—III), experimental values of the z_r are available only for (I). We have therefore used the same values for the displacements of the four atoms (two hydrogen and two carbon) in the overcrowded region in both (II) and (III). As it will appear that the

[3] Clar and Ironside, *Proc. Chem. Soc.*, 1958, 150.

deformation energy is almost the same in all three molecules, this serves *a posteriori* to justify our assumption of equal displacements in the overcrowded regions. This is all the more likely since the actual displacements in the overcrowded region are determined very largely by the repulsive overlap forces between the charge-clouds of the non-bonded atoms. In going from (I) to (II) to (III) we might have expected slightly smaller displacements than in (I). But the repulsive energy increases very rapidly as the atoms get closer together. Hence the balance between repulsive energy and overcrowding energy is expected to occur with almost the same displacements in the overcrowded region in all three cases. Thus we shall take:

z for overcrowded carbon = 1·32 Å; z for overcrowded hydrogen = 1·36 Å

Our problem therefore reduces to finding the minimum value of the quadratic function $V(z_r)$ with the restriction that in the overcrowded region the z-values have the numerical



(I) (II) (III)

values shown above. Thus we have to solve the set of equations $\partial V/\partial z_r = 0$. When this is done, and the z_r have been calculated, the deformation energy is simply $\frac{1}{2}\sum_{\substack{\text{overcrowded}\\\text{atoms}}} z_r(\partial V/\partial z_r)$.

The total strain energy, of course, is the sum of this deformation energy and the repulsive overlap energy between the atoms of the overcrowded region.

The latter will be a constant in all our calculations, though its precise value must remain unknown until we possess more information about the interatomic forces. Our calculations were made on a Ferranti Pegasus electronic computer. This machine could be programmed, not only to write down and solve the equations, but also to make the final calculations of the deformation energy.

Results for Molecules (I—III).—Tables 1 and 3 show both the actual predicted displacements (in Å) and the deformation energy. Column 3 of Table 1 is a recalculated version of the Coulson–Senent work in ref. 2, and, apart from one copying mistake (the $C_{(2)}$ atom in the phenanthrene region for which the true value is 0·95 Å, whereas the previously reported value was 1·95 Å) the two calculations agree excellently.

It will be seen that the displacements and the deformation energy in these molecules are very similar. The displacements far away from the overcrowded region, though somewhat different, appear to make very little contribution to the deformation energy. Thus the rigidity of the molecular framework has virtually no influence on the displacements in and near to the overcrowded region.

Application to Tetrabenzoperopyrene (IV).—There are two ways in which the overcrowding can be relieved. In the first, the atoms on one side of the axis (b) have positive displacements, and those on the other side have negative ones. This set of displacements is symmetrical about the axis (a). But in the other scheme, it is almost as if the top half of the molecule were rotated in one direction around the axis (a), and the bottom half were rotated in the opposite direction: the result is a kind of propeller-shape. Both possibilities must be considered. The more probable configuration will then be that which gives rise to the lower energy of deformation V. In both cases there are 42 planarity terms and 52 torsion terms, though the number of simultaneous linear equations to be

TABLE 1. *Calculations of z_r (in Å) for molecules* (I—IV).

Atom	(I) (Coulson and Senent)	(I) (Present calcn.)	(II)	(III)	(IV) (First config.)	(IV) (Second config.)
1	0·11	0·114	0·117	0·128	1·716	0
2	0·33	0·316	0·197	0·248	1·549	0·373
3	0·63	0·619	0·458	0·515	1·153	0·348
4	0·95	0·946	0·680	0·715	1·189	0·765
5	1·12	1·109	0·641	0·659	1·697	1·311
6	1·62	1·644	0·950	0·963	1·985	1·856
7	1·96	1·993	1·104	1·110	1·846	1·887
8	1·85	1·873	1·630	1·637	(1·32)	(1·32)
9	(1·32)	(1·32)	1·976	1·981	0·861	0·675
10	0·85	0·823	1·864	1·865	0·291	0·155
11	0·27	0·258	(1·32)	(1·32)	0·474	0
12	0·20	0·197	0·824	0·826	0·917	0
13	0·61	0·610	0·262	0·263	2·026	0
14	1·16	1·176	0·328	0·336	1·751	0·670
15	1·79	1·827	0·046	0·118	1·916	1·344
16	2·36	2·418	0·505	0·591	2·391	2·288
17	2·19	2·231	0·908	0·949	2·171	2·349
18	(1·36)	(1·36)	1·184	1·203	(1·36)	(1·36)
19			1·809	1·819		
20			2·394	2·400		
21			2·219	2·220		
22			(1·36)	(1·36)		
23				0·212		

TABLE 2. *Calculated and observed displacements* (10^{-3} Å) *for chrysene* (V) *and 20-methylcholanthrene* (VI).*

Atom	(V) obs.	(V) calc. approx. *a*	(V) calc. approx. *b*	(VI) obs.	(VI) calc. approx. *a*	(VI) calc. approx. *b*
1	−4			+25		
2	+1			+20		
3	+5			−9		
4	+4			−28		
5	+2			−18		
6	−13			+5		
7	−3			+15		
8	+10			+10		
9	+9			−2		
10	+4			+2		
11	−1			+6		
12	−5			−11		
13	−4			+23		
14	−2			+10		
15	+13			+1		
16	+3			−17		
17	−10			−25		
18	−9			−5		
19		−1·0	+1		+50	+55
20		+6·0	+7		+35	+52
21		+1	+11		−35	−56
22		−24	−33		−24	−30
23		−7	−6		−1	+9
24		+15	+17		−26	−74
25		+1	−2		+2	−6
26		−6	−8		−32	−41
27		−1	−11		−12	−3
28		+24	+33	+18		
29		+7	+6	+4		
30		−15	−17	−25		

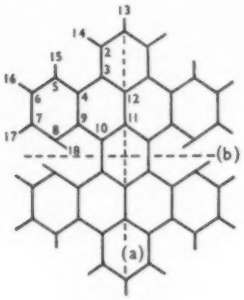
* + and − signs indicate displacements above and below the mean plane of the molecule.

TABLE 3. *Deformation energies* (kcal./mole).

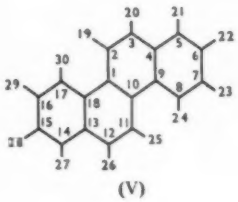
(I)		17·9 *, 17·98 †	(V)	(Approx. *a*)	0·025
(II)		18·54	(V)	(Approx. *b*)	0·040
(III)		18·60	(VI)	(Approx. *a*)	0·155
(IV)	(First Config.)	41·5	(VI)	(Approx. *b*)	0·260
(IV)	(Second Config.)	36·3			

* Ref. 1. † Present calcn.

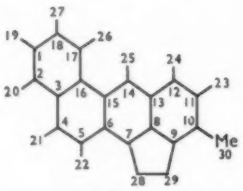
solved is about one-quarter of the sum (42 + 52 = 94) on account of the two symmetry axes. The results are shown in Tables 1 and 3. Now despite the fact that the C.S. potential function neglects certain cross-terms, it seems entirely reasonable that the true sequence of deformation energies should be as in these calculations. We are therefore led to propose the second, *i.e.*, propeller, shape for this molecule. If the calculated energy difference between the two tautomeric forms is taken to be the true value, then less than 1 in 10^4 molecules would be found in the alternative shape at room temperature.



(IV)



(V)



(VI)

Molecular Crystals: Chrysene and 20-Methylcholanthrene.—Iball [4] has found that, in their crystalline form, chrysene and 20-methylcholanthrene are slightly buckled. The observed displacements z_r of the various atoms are shown in Table 2 [see (V) and (VI) for system of numbering used] measured in units of 10^{-3} Å. These are, admittedly, small displacements but a statistical test, for which we are grateful to Dr. J. S. Rollett, shows that they are almost certainly significant. They must be the result of intermolecular forces, associated with the molecular packing. These may be partly attractive dispersion forces and partly repulsive overlap forces, with the former predominating. It is of some interest to estimate the energy involved in these deformations. This cannot be done by direct evaluation of the potential energy function $V(z_1 \ldots)$ because only the positions of the carbon atoms are known. The experimental analysis was not sufficiently detailed to pick out the hydrogen atoms. But the value of $V(z_1 \ldots)$ depends rather seriously upon the hydrogen displacements. We have therefore adopted two independent sets of assumptions, between which the truth is almost certain to lie. In (*a*) we suppose that the intermolecular forces act only on the hydrogen atoms. Then $\partial V/\partial z_r = 0$ for each carbon atom, but not for the hydrogens. This set of equations, coupled with the known carbon-atom displacements, can then be used to calculate the positions of the hydrogen atoms, and also the value of V. In (*b*) we suppose that the intermolecular forces act only on the carbon atoms, so that $\partial V/\partial z_r = 0$ for each hydrogen, but not for carbon. Again we calculate the positions of the hydrogen atoms, and the value of V. Since there are more carbon than hydrogen atoms, there are more equations than unknowns in method (*a*). In that situation a least-squares procedure was used to find the best z_r. Since the relative uncertainties in the measured carbon-atom displacements are quite large, this procedure seems entirely reasonable.

When writing down the C.S. potential for methylcholanthrene the following approximations were introduced. (1) We neglect strain in the 5-membered saturated ring, since this is not likely to distort the molecule in an out-of-plane direction. (2) To permit us to write down planarity terms associated with the carbon atoms where the 5-ring joins the aromatic framework, we replace the saturated part of the 5-ring by two hypothetical carbon atoms at a valency angle of 120°. The 20-methyl group is similarly replaced by a hydrogen atom at the appropriate distance.

[4] Iball, personal communication.

The results of the two calculations (*a*) and (*b*) are shown in Tables 2 and 3. In all cases the deformation energy is very small, being of the order of one-hundredth part of the sublimation energy. Thus it is easy to see that out-of-plane displacements of this magnitude (or even rather larger) may arise in the process of packing the separate molecules into the crystal. Indeed it seems likely that such degrees of non-planarity may be more common than has hitherto been suspected. Highly accurate *X*-ray analysis may reveal more of these cases in the future. Some words of J. M. Robertson [5] seem appropriate: "The molecule (anthracene) which we proved planar in 1932 and much more accurately planar in 1950, is now found to be non-planar. The carbon atom 9 in anthracene deviates most from the mean plane, by 0·012 Å. This is the carbon atom which is approached directly by a hydrogen atom from a neighbouring molecule."

Our sincere thanks are offered to Dr. Iball for providing us with the observed displacements in chrysene and methylcholanthrene in advance of publication; to Dr. J. S. Rollett for much helpful discussion and for the programme by which we determined the deformation and the energy on the Pegasus computer; and to Messrs. Ferranti for allowing us machine time for these calculations. One of us (M. A. A.) also acknowledges the West Bengal Lytton Moslem Scholarship from the Government of West Bengal.

MATHEMATICAL INSTITUTE, OXFORD. [*Received, November 24th*, 1958.]

[5] Robertson, *Rev. Mod. Phys.*, 1958, **30**, 158.

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301. *Internuclear Cyclisation. Part XIII.* The Decomposition of Diazonium Salts prepared from* N-o-*Aminobenzoyldiphenylamines. A New Molecular Rearrangement.*

By D. H. HEY and T. M. MOYNEHAN.

Thermal decomposition of an aqueous solution of the diazonium chloride from *N-o*-aminobenzoyldiphenylamine gives 10-phenylphenanthridone and *N-o*-hydroxybenzoyldiphenylamine, but catalytic decomposition at room temperature by the addition of copper powder gives 10-phenylphenanthridone and diphenyl-2-carboxyanilide. Evidence on the nature of the anilide-forming rearrangement is provided by the study of similar reactions with the *N-o*-aminobenzoyl derivatives of di-*p*-tolylamine, 4-methyldiphenylamine, and 4-chlorodiphenylamine. The rearrangement occurs only in the catalytic decomposition of the diazonium salt.

As part of a study of the Pschorr and related reactions the decomposition of diazonium salts from *N-o*-aminobenzoyldiphenylamines (I) was studied. Unsymmetrically substituted compounds of this type (*i.e.*, R ≠ R′) can cyclise with either aromatic ring attached to the nitrogen atom; the products should provide useful evidence of the effect of substituent atoms or groups in one or both of these rings on the ring-closure.

N-o-Aminobenzoyldiphenylamine (I; R = R′ = H) was obtained by reduction of *N-o*-nitrobenzoyldiphenylamine, prepared from *o*-nitrobenzoyl chloride and diphenylamine. When its diazonium chloride was decomposed by heating the aqueous solution, the products were 10-phenylphenanthridone (II; R = R′ = H) and *N-o*-hydroxybenzoyldiphenylamine. The identity of the former was at first in question because it had m. p. 225°, whereas Walls [1] had claimed to have prepared this compound by heating 9-bromophenanthridine with phenol and had recorded m. p. 118—119°. It seemed possible that Walls's compound might be 9-phenoxyphenanthridine (V; R = H) and this was confirmed when it was found that the compound of m. p. 118—119°, on being heated at 360°,

* Part XII, *J.*, 1957, 1781.

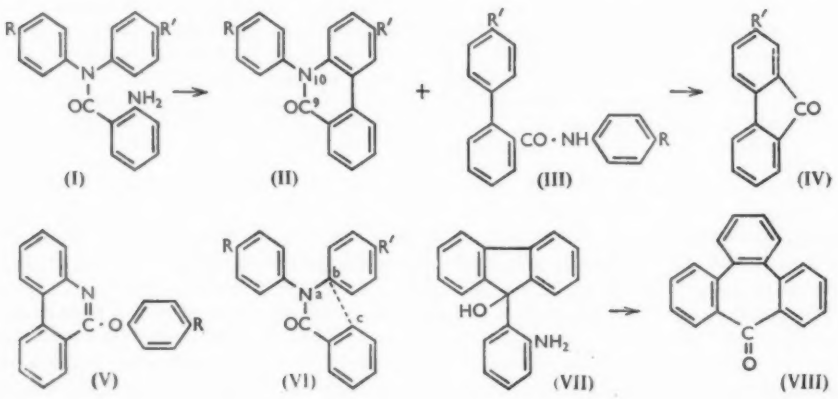
[1] Walls, *J.*, 1934, 104.

XUM

rearranged to a compound, m. p. 225°, identical with our product. This rearrangement is analogous to Chapman's synthesis of diphenylamine [2] in which phenyl *N*-phenylbenzimidate is converted by heat into *N*-benzoyldiphenylamine. When, however, the aqueous diazonium chloride prepared from *N*-*o*-aminobenzoyldiphenylamine was decomposed at room temperature by addition of copper powder, the product consisted of 10-phenylphenanthridone and diphenyl-2-carboxyanilide (III; R = R′ = H). The constitution of the latter was confirmed by its identity with an authentic specimen and by conversion into fluorenone after being heated with phosphoric acid. A similar result was obtained when the diazonium fluoroborate from *N*-*o*-aminobenzoyldiphenylamine was decomposed in acetone by addition of copper powder.

The unexpected formation of the anilide (III) is clearly due to a new type of molecular rearrangement in which an aryl group migrates from the nitrogen atom to the nuclear position to which the diazonium group was originally attached. There are two possible routes for such a rearrangement. The nuclear position from which the diazonium group has been eliminated (VI, c) can become attached either to the *ortho*-position of one of the *N*-phenyl groups, followed by fission of the C–N bond (ab), or to one of the *N*-phenyl groups at the position of attachment of the nitrogen atom, again followed by fission of the C–N bond (as in VI). A decision was made by carrying out the reaction with *N*-*o*-aminobenzoyldi-*p*-tolylamine (I; R = R′ = Me), prepared from di-*p*-tolylamine and *o*-nitrobenzoyl chloride, and subsequent reduction. Decomposition of the diazonium chloride with copper powder in aqueous solution gave 3-methyl-10-*p*-tolylphenanthridone (II; R = R′ = Me) and 4-methyldiphenyl-2′-carboxy-*p*-toluidide (III; R = R′ = Me), identical with an authentic specimen. The formation of this toluidide proves that the second route (VI) has been followed; the alternative would give a toluidide of 3-methyldiphenyl-2′-carboxylic acid.

When the diazonium fluoroborate from *N*-*o*-aminobenzoyldi-*p*-tolylamine was decomposed in acetone by copper powder a product was obtained which did not yield to separation by chromatography. On being heated with phosphoric acid, however, the product gave 3-methyl-10-*p*-tolylphenanthridone (II; R = R′ = Me) (which is not affected by this



treatment) and 2-methylfluorenone (IV; R′ = Me), which must have been derived from 4-methyldiphenyl-2′-carboxy-*p*-toluidide (III; R = R′ = Me). When an aqueous solution of the diazonium chloride from *N*-*o*-aminobenzoyldi-*p*-tolylamine was heated (without copper powder) an intractable mixture was obtained which, when treated with hot phosphoric acid, gave only 3-methyl-10-*p*-tolylphenanthridone. No 2-methylfluorenone

[2] Chapman, *J.*, 1927, 1743.

was formed, and therefore under these conditions no rearrangement can have occurred. Authentic specimens of both 3- and 4-methyldiphenyl-2′-carboxy-*p*-toluidide were prepared from the appropriate iodotoluene and methyl *o*-iodobenzoate by an Ullmann reaction, followed by hydrolysis to the acid and thence to the *p*-toluidide.

The rearrangement described above bears a superficial resemblance to another reported by Stiles and Libbey,[3] to which brief reference has been made elsewhere.[4] These authors reported that the decomposition of the diazonium sulphate from 9-*o*-aminophenyl-9-fluorenol (VII) gave, in addition to the phenol, tribenzotropone (VIII) in 24% yield.

In both this rearrangement and the one now reported the nuclear position from which the nitrogen is eliminated attacks a second nucleus at the point of attachment of an extra-nuclear carbon or nitrogen atom with subsequent fission of a carbon–carbon or carbon–nitrogen bond respectively. The two rearrangements, however, differ in that Stiles and Libbey's proceeds on warming the aqueous diazonium solution, whereas ours only proceeds in the cold by addition of copper powder.

With an unsymmetrically substituted *o*-aminobenzoyldiphenylamine (*e.g.*, I; R ≠ R′) the decomposition of the diazonium chloride could in the absence of copper powder give a mixture of two isomeric 10-arylphenanthridones, and in the presence of copper powder a mixture of two isomeric diphenyl-2-carboxyanilides in addition. In order to test to what extent these possibilities are realised, reactions have been carried out with *N*-*o*-aminobenzoyl-4-methyldiphenylamine (I; R = Me, R′ = H) and *N*-*o*-aminobenzoyl-4-chlorodiphenylamine (I; R = Cl, R′ = H). 4-Methyl- and 4-chloro-diphenylamine, prepared from benz-*p*-toluidide and benz-*p*-chloroanilide respectively by Chapman's method,[2] were converted into the *o*-aminobenzoyl derivatives. With both of these monosubstituted *N*-*o*-aminobenzoyldiphenylamines, the thermal decomposition of the diazonium salts in aqueous solution gave only phenanthridones, but the decomposition at room temperature in the presence of copper powder gave mixtures of phenanthridones and diphenyl-2′-carboxyanilides. Treatment of these mixtures with hot phosphoric acid converted the anilides into fluorenones. The mixtures of fluorenones thus obtained could not be separated but were analysed spectrophotometrically by Dewar and Urch's method.[5] In order to distinguish between the two pairs of 10-arylphenanthridones formed one member of each pair was synthesised by treating 9-chlorophenanthridine with *p*-cresol and isomerising the *p*-tolyloxyphenanthridine (V; R = Me) produced, by heat, to 10-*p*-tolylphenanthridone (II; R = Me; R′ = H); and similarly 10-*p*-chlorophenylphenanthridone (II; R = Cl; R′ = H) from 9-*p*-chlorophenoxyphenanthridine (V; R = Cl).

In order to express the ratios in which the isomeric anilides are formed in terms of the observed ratios of the fluorenones based on spectrophotometry, it was necessary to determine in what yields the anilides were converted into the fluorenones under our conditions. The four anilides concerned [diphenyl-2-carboxy-*p*-toluidide (III; R = Me; R′ = H), 4-methyldiphenyl-2′-carboxyanilide (III; R = H; R′ = Me), diphenyl-2-carboxy-*p*-chloroanilide (III; R = Cl; R′ = H), and 4-chlorodiphenyl-2′-carboxyanilide (III; R = H; R′ = Cl)] were prepared and under the standard treatment with hot phosphoric acid gave the appropriate fluorenones in yields of 96·8%, 95%, 97·2%, and 98% respectively. These values were used in calculating the yields of the anilides formed in the reactions with the monosubstituted *o*-aminobenzoyldiphenylamines.

In the thermal and catalytic decomposition of the diazonium chloride from *N*-*o*-aminobenzoyl-4-methyldiphenylamine (I; R = Me; R′ = H) only one phenanthridone was isolated. With *N*-*o*-aminobenzoyl-4-chlorodiphenylamine the catalytic decomposition gave the two phenanthridones in approximately equal amounts, whereas in the thermal decomposition the major product was 10-*p*-chlorophenylphenanthridone (II; R = Cl; R′ = H). This result is in agreement with the representation of the catalytic reaction

[3] Stiles and Libbey, *J. Org. Chem.*, 1957, **22**, 1243.
[4] Hey and Moynehan, *Proc. Chem. Soc.*, 1957, 209.
[5] Dewar and Urch, *J.*, 1957, 345.

as a homolytic process, whereas in the thermal decomposition the deactivation of the nucleus containing the chlorine atom indicates a heterolysis. With none of the four amines did thermal decomposition of an aqueous solution of the diazonium salt give any product of rearrangement, whereas in all four cases the catalysed reaction produced the

Base	Method *	Phenanthridone		Anilide	
N-*o*-Aminobenzoyldiphenylamine	*A* i	10-Phenyl-	(62%)	—	
,,	*B*	,,	(40%)	Diphenyl-2-carboxyanilide	(45%)
,,	*C*	,,	(33·5%)	,,	(18·5%)
N-*o*-Aminobenzoyldi-*p*-tolylamine	*A* i	3-Methyl-10-*p*-tolyl-	(22%)	—	
,,	*B*	,,	(28%)	4-Methyldiphenyl-2′-carboxy-*p*-toluidide	(58%)
,,	*C*	,,	(31·5%)	,,	(36%) †
N-*o*-Aminobenzoyl-4-methyldiphenylamine	*A* i	10-*p*-Tolyl-	(9%)	—	
,,	*B*	,,	(14·5%)	4-Methyldiphenyl-2′-carboxyanilide	(28·4%) †
				Diphenyl-2-carboxy-*p*-toluidide	(25·2%) †
N-*o*-Aminobenzoyl-4-chlorodiphenylamine	*A* ii	10-*p*-Chlorophenyl-	(24%)	—	
		3-Chloro-10-phenyl-	(12%)		
,,	*B*	10-*p*-Chlorophenyl-	(17%)	4-Chlorodiphenyl-2′-carboxyanilide	(19%) †
		3-Chloro-10-phenyl-	(19%)	Diphenyl-2-carboxy-*p*-chloroanilide	(21%) †

* *A*, Action of heat on aqueous diazonium (i) chloride, (ii) sulphate. *B*, Action of copper powder on aqueous diazonium chloride or *C*, on diazonium fluoroborate in acetone.
† Yield calculated by conversion into corresponding fluorenone.

rearrangement. The analyses of the mixtures of fluorenones obtained from the anilides showed that the presence of substituents has no marked effect upon this reaction, which result may be taken as indicative of a homolytic mechanism for the rearrangement (cf. de Tar [6]). Attempts to prepare 4-methoxycarbonyl-*N*-*o*-nitrobenzoyldiphenylamine, for a similar sequence of reactions with a methoxycarbonyl substituent, were unsuccessful.

The yields of the products obtained in the reactions investigated are tabulated.

Experimental

Unless otherwise stated, light petroleum had b. p. 60—80°.

N-o-*Aminobenzoyldiphenylamine.*—Ethereal *o*-nitrobenzoyl chloride (6 g. in 20 ml.) was added slowly to diphenylamine (6 g.) in pyridine (15 ml.) and dry ether (50 ml.), and the mixture boiled under reflux for 1 hr. After removal of the ether, water was added, and recrystallisation from ethanol (charcoal) of the brown solid which separated gave N-o-*nitrobenzoyldiphenylamine* (10·3 g.), pale green plates, m. p. 158—159° (Found: C, 72·3; H, 4·3. $C_{19}H_{14}O_3N_2$ requires C, 71·7; H, 4·4%). A solution of this (8 g.) in benzene (150 ml.) with Raney nickel (8 g.) was hydrogenated at room temperature and pressure. The catalyst was filtered off and the solution concentrated. Recrystallisation of the residual white solid from benzene gave N-o-*aminobenzoyldiphenylamine* (6·4 g.) in needles, m. p. 178—179° (Found: C, 79·8; H, 5·5. $C_{19}H_{16}ON_2$ requires C, 79·2; H, 5·6%).

Thermal Decomposition in Aqueous Solution of the Diazonium Chloride from N-o-*Aminobenzoyldiphenylamine.*—The amine (3·5 g.), suspended in concentrated hydrochloric acid (20 ml.) and water (40 ml.), was diazotised at 0° with sodium nitrite (1 g.) in water (10 ml.). This was stirred at 0° for 1 hr., then urea (1 g.) was added, and the solution diluted to 250 ml. and warmed to 80° for 1 hr. A pale fawn solid separated which was filtered off and dissolved in chloroform. The filtrate was extracted with chloroform and the combined chloroform solutions were washed with 10% aqueous sodium hydroxide and dried (Na_2SO_4). Removal

[6] de Tar, *Organic Reactions*, 1957, **9**, 409.

of the solvent left a pale brown solid which was recrystallised from benzene to give 10-*phenylphenanthridone* (1·625 g.), needles, m. p. 225° (Found: C, 83·8; H, 5·0. $C_{19}H_{13}ON$ requires C, 84·1; H, 4·8%). The mother-liquor (50 ml.) was poured on an alumina column (100 g.). Elution with benzene (1 l.) and benzene–ether (3 : 1; 300 ml.) gave more 10-phenylphenanthridone (0·44 g.). Ether (500 ml.) gave a second product, prisms (0·14 g.), m. p. 197—199° (Found: C, 78·8; H, 5·5; N, 4·75%). Elution with methanol gave a red-brown tar (0·12 g.). The alkali washings were acidified and extracted with chloroform. Concentration of the dried (Na_2SO_4) extract left a brown resin which crystallised from ethanol to give *N-o*-hydroxybenzoyldiphenylamine (0·87 g.), prisms, m. p. 192° (Cohn [7] recorded m. p. 193°).

Catalytic Decomposition of the Diazonium Chloride from N-o-*Aminobenzoyldiphenylamine.*—The amine (2·0 g.) was diazotised as described in the previous experiment, and the solution diluted to 200 ml. Copper powder (3 g.) was added, which caused vigorous evolution of nitrogen. After 1 hr. the solution no longer gave a positive test with alkaline β-naphthol. The mixture was filtered and both filtrate and residue extracted with chloroform, whose removal from the dried (Na_2SO_4) extract left a yellow gum which solidified on standing. Recrystallisation from benzene gave 10-phenylphenanthridone (0·63 g.), needles, m. p. 225°. The mother-liquor was poured on alumina (90 g.). Elution with benzene–light petroleum (1 : 1) (300 ml.) and benzene (500 ml.) gave diphenyl-2-carboxyanilide (0·85 g.), needles, m. p. 109—110°, from light petroleum, identical with an authentic specimen. After being heated at 150° for 2 hr. with 100% phosphoric acid, diphenyl-2-carboxyanilide gave fluorenone, m. p. and mixed m. p. 83°. Further elution with benzene (400 ml.) and benzene–ether (2 : 1) (200 ml.) gave more 10-phenylphenanthridone (0·13 g.), needles, m. p. 225°, from light petroleum. Elution with ether and methanol gave a yellow gum (0·16 g.) which could not be crystallised.

Catalytic Decomposition of the Diazonium Fluoroborate from N-o-*Aminobenzoyldiphenylamine.*—The amine (2·0 g.) was diazotised as above and an aqueous solution of sodium fluoroborate (5 g. in 20 ml.) was added slowly to the cold diazonium solution and the mixture stirred for a few minutes. The yellow diazonium fluoroborate was filtered off, washed with cold water (3 × 10 ml.), and dried *in vacuo* overnight. Copper powder (3 g.) was added to the fluoroborate (2·6 g.) in acetone (200 ml.), and the solution stirred for 48 hr. Nitrogen was evolved slowly. The mixture was filtered into water and both filtrate and residue were extracted with chloroform. After removal of the chloroform from the dried (Na_2SO_4) extract, the residue was recrystallised from benzene to give 10-phenylphenanthridone (0·41 g.), needles, m. p. 225°. The mother-liquor (50 ml.) was adsorbed on an alumina column (80 g.). Elution with benzene–light petroleum (1 : 1) (1 l.) gave diphenyl-2-carboxyanilide (0·35 g.), m. p. 108—109°. Further elution with benzene–light petroleum (2 : 1) (600 ml.) gave 10-phenylphenanthridone (0·22 g.), needles, m. p. 225°, from ethanol. Elution with benzene (1200 ml.) gave colourless plates (0·60 g.), m. p. 204—206°, from ethanol (Found: C, 79·2; H, 4·7; N, 4·6%; *M*, 232), which formed a 2 : 4-dinitrophenylhydrazone, orange needles, m. p. 204—206°, from ethyl acetate (Found: C, 63·5; H, 3·9%). Elution with ether and methanol gave a red tar (0·10 g.) which could not be crystallised.

9-*Phenoxyphenanthridine* (*cf. ref.* 1).—9-Chlorophenanthridine [8] (1 g.) was heated with phenol (10 g.) at 150° for 1 hr. Addition of excess of sodium hydroxide solution gave a yellow precipitate which crystallised from ethanol to give 9-*phenoxyphenanthridine* (1·15 g.), needles, m. p. 117—118° (Found: C, 84·1; H, 4·7. $C_{19}H_{13}ON$ requires C, 84·1; H, 4·8%). Walls [1] who incorrectly described this compound as 10-phenylphenanthridone, recorded m. p. 118—119°.

10-*Phenylphenanthridone.*—9-Phenoxyphenanthridine (0·5 g.) was heated at 350° for 2 hr. Recrystallisation of the resultant dark brown solid from ethanol (charcoal) gave 10-phenylphenanthridone (0·3 g.), needles, m. p. 225°, identical with the product obtained as above.

N-o-*Aminobenzoyldi*-p-*tolylamine.*—As described for *N-o*-nitrobenzoyldiphenylamine, di-*p*-tolylamine (5 g.) and *o*-nitrobenzoyl chloride (6 g.) in presence of pyridine (10 ml.) and ether (50 ml.) gave N-o-*nitrobenzoyldi*-p-*tolylamine* (7·9 g.), pale yellow plates, m. p. 142—144°, from benzene (Found: C, 73·2; H, 4·9. $C_{21}H_{18}O_3N_2$ requires C, 72·8; H, 5·2%). A solution of this (7·5 g.) in benzene (150 ml.) with Raney nickel (6 g.) was hydrogenated at room temperature and pressure. The catalyst was filtered off and the residue, after removal of the solvent, crystallised from ethanol to give N-o-*aminobenzoyldi*-p-*tolylamine* (6·3 g.), needles, m. p. 166° (Found: C, 79·7; H, 6·3. $C_{21}H_{20}ON_2$ requires C, 79·7; H, 6·3%).

[7] Cohn, *J. prakt. Chem.*, 1900, **61**, 548.
[8] Graebe and Wander, *Annalen*, 1893, **276**, 245.

XUM

3-*Methyldiphenyl*-2′-*carboxylic Acid*.—Methyl *o*-iodobenzoate (10 g.), *m*-iodotoluene (10 g.), and copper bronze (20 g.) were stirred and heated in a metal-bath at 210°. After 1 hr. the temperature of the bath was gradually raised to 260° and kept thereat until the mixture stopped boiling and maintained at the same temperature for a further hour. The mixture was cooled and extracted with hot ethanol. This extract (150 ml.) was refluxed for 2 hr. with potassium hydroxide (20 g.) in water (20 ml.). Most of the solvent was distilled off, and the residue diluted with water, washed with ether, and acidified with hydrochloric acid. The precipitate was extracted with cold benzene (3 × 20 ml.) and left a residue of diphenic acid. Removal of the benzene left a yellow gum, which crystallised from light petroleum to give 3-*methyldiphenyl*-2′-*carboxylic acid* (1·1 g.), needles, m. p. 100—101° (Found: C, 79·4; H, 5·6. $C_{14}H_{12}O_2$ requires C, 79·25; H, 5·6%).

3-*Methyldiphenyl*-2′-*carboxy*-p-*toluidide*.—A solution of the acid (0·2 g.) in thionyl chloride (5 ml.) was refluxed for 30 min. Excess of thionyl chloride was removed and the residue dissolved in dry benzene (10 ml.). *p*-Toluidine (0·3 g.) was added, and the mixture warmed on a water-bath for 15 min., then diluted with ether, washed with dilute aqueous acid, and alkali, and dried (Na_2SO_4). The residue, after removal of the solvent, crystallised from light petroleum to give 3-*methyldiphenyl*-2′-*carboxy*-p-*toluidide* (0·2 g.), needles, m. p. 105° (Found: C, 83·8; H, 6·2. $C_{21}H_{19}ON$ requires C, 83·7; H, 6·3%).

4-*Methyldiphenyl*-2′-*carboxylic Acid*.—Methyl *o*-iodobenzoate (10 g.), *p*-iodotoluene (10 g.), and copper bronze (20 g.) were treated as for the 3-isomer. After separation from diphenic acid by extraction with cold benzene, the solvent was removed and the brown residue recrystallised from benzene to give 4-*methyldiphenyl*-2′-*carboxylic acid* (1·5 g.), prisms, m. p. 147—149° (Found: C, 79·4; H, 5·8. $C_{14}H_{12}O_2$ requires C, 79·25; H, 5·6%).

4-*Methyldiphenyl*-2′-*carboxy*-p-*toluidide*.—4-Methyldiphenyl-2′-carboxylic acid, heated with thionyl chloride, as for the 3-isomer, gave 2-methylfluorenone, yellow needles, m. p. 91—92° from light petroleum (b. p. 40—60°). Kruber [9] recorded m. p. 92°. Therefore, the acid (0·2 g.) and *p*-toluidine (0·5 g.) were heated at 200° for 2 hr. The product was dissolved in ether, washed with dilute aqueous acid, and alkali, and dried (Na_2SO_4). After removal of the solvent the residue gave 4-*methyldiphenyl*-2′-*carboxy*-p-*toluidide* (0·08 g.), needles, m. p. 134—135°, from light petroleum (Found: C, 83·7; H, 6·4. $C_{21}H_{19}ON$ requires C, 83·7; H, 6·3%).

Catalytic Decomposition of the Diazonium Chloride from N-o-*Aminobenzoyldi*-p-*tolylamine*.—The amine (3·5 g.), suspended in hydrochloric acid (15 ml.) and water (40 ml.), was diazotised at 0° with sodium nitrite (1 g.) in water (10 ml.). This was stirred at 0° for 1 hr., then urea (1 g.) was added, and the solution diluted to 250 ml. Addition of copper powder (5 g.) caused vigorous evolution of nitrogen and a cream solid separated. After 2 hr. the mixture was filtered and filtrate and residue were extracted with chloroform. The extract was washed with sodium hydroxide solution and dried (Na_2SO_4). Removal of the chloroform left a yellow gum which was dissolved in benzene (50 ml.) and adsorbed on alumina (100 g.). Elution with benzene–light petroleum (1 : 1) (200 ml.) gave 4-methyldiphenyl-2′-carboxy-*p*-toluidide (0·6 g.), needles, m. p. 134—135°, from light petroleum, identical with the authentic specimen. Further elution with benzene–light petroleum (1 : 1) (200 ml.) and benzene (600 ml.) gave a mixture. Benzene–ether and ether gave a brown tar (0·08 g.) and methanol gave a small amount of yellow gum. The mixture was dissolved in benzene and adsorbed on silica gel (70 g.). Elution with benzene–light petroleum (1 : 2) (600 ml.) and (1 : 1) (300 ml.) gave 4-methyldiphenyl-2′-carboxy-*p*-toluidide (1·35 g.). Benzene (800 ml.) gave 3-*methyl*-10-p-*tolylphenanthridone* (0·93 g.), needles, m. p. 175—176°, from light petroleum (Found: C, 84·1; H, 5·7. $C_{21}H_{17}ON$ requires C, 84·3; H, 5·7%). Ether gave a little yellow gum.

Catalytic Decomposition of the Diazonium Fluoroborate from N-o-*Aminobenzoyldi*-p-*tolylamine*.—The amine (3·7 g.) was diazotised as above, and aqueous sodium fluoroborate (6 g. in 20 ml.) added to the cold diazonium solution. The yellow diazonium fluoroborate was filtered off and washed with cold water. It began to darken on standing and so it was immediately dissolved in acetone (200 ml.), and copper powder (5 g.) added. A vigorous evolution of nitrogen occurred. After 2 hr. the mixture was filtered into water and both filtrate and residue were extracted with chloroform, whose removal from the dried (Na_2SO_4) extract left an orange gum, which was dissolved in benzene (50 ml.) and adsorbed on silica gel (70 g.). Elution with benzene–light petroleum (1 : 2) (400 ml.) and (2 : 1) (1200 ml.) gave a white solid (2·7 g.), which melted over a wide range. Benzene (200 ml.) gave a yellow gum (0·25 g.) which could not be

[9] Kruber, *Ber.*, 1932, **65**, 1394.

crystallised. Further elution with benzene (300 ml.) and benzene–ether (1 : 1) (400 ml.) gave prisms (0·43 g.), m. p. 196°, from benzene (Found: C, 82·9; H, 6·2; N, 5·05%; *M*, 225), which was not a ketone. Elution with ether and methanol gave a small amount of brown tar. The mixture obtained by elution with benzene–light petroleum was heated with 100% phosphoric acid (30 g.) at 150° for 2 hr. Water was added and the mixture extracted with chloroform whose removal from the dried (Na_2SO_4) extract left a dark brown glass, which was dissolved in benzene (20 ml.) and adsorbed on alumina (80 g.). Elution with benzene–light petroleum (1 : 10) (700 ml.) gave 2-methylfluorenone (0·82 g.), yellow needles, m. p. 91—92°, from light petroleum (b. p. 40—60°). Benzene–light petroleum (1 : 1) (300 ml.) and benzene (1 l.) gave 3-methyl-10-*p*-tolylphenanthridone (1·1 g.), needles, m. p. 174—175°, from light petroleum. Ether gave a little brown tar.

Thermal Decomposition in Aqueous Solution of the Diazonium Chloride from N-o-*Aminobenzoyldi*-p-*tolylamine.*—The amine (3 g.) was diazotised as above and the diazonium solution diluted to 250 ml. and warmed at 80° for 1 hr. A brown oil separated. The mixture was extracted with chloroform and this extract dried (Na_2SO_4) and concentrated. The residual pale brown gum was dissolved in benzene and adsorbed on alumina (100 g.). Elution with benzene–light petroleum, benzene, and benzene–ether, all gave a white solid melting over a wide range. Methanol gave a brown tar (0·75 g.) which could not be crystallised. The solid was heated with 100% phosphoric acid (15 g.) at 150° for 2 hr. Water was added, and the mixture extracted with chloroform whose removal from the dried (Na_2SO_4) extract left a brown resin, which was dissolved in benzene and adsorbed on alumina (80 g.). Elution with benzene–light petroleum (1 : 3) (200 ml.) gave a little orange solid, m. p. >300°. Benzene (500 ml.) gave 3-methyl-10-*p*-tolylphenanthridone (0·48 g.), needles, m. p. 174—175°, from light petroleum. Benzene–ether (3 : 1) (600 ml.) gave a brown gum (0·925 g.), which yielded more 3-methyl-10-*p*-tolylphenanthridone (0·14 g.) on extraction with light petroleum.

4-*Methyldiphenylamine* (*cf. ref.* 2).—Benz-*p*-toluidide (42·4 g.) and phosphorus pentachloride (43 g.) were heated on a water-bath until no more hydrogen chloride was evolved. The phosphorus oxychloride was distilled off under reduced pressure and the yellow residue was dissolved in ether. Sodium (5·05 g.) in ethanol (200 ml.) was cooled in ice, and phenol (22·5 g.) added. Immediately it had dissolved the ethereal solution of the benzimidoyl chloride was added and the mixture kept overnight. The residue, after removal of the solvent, was washed with water to remove sodium chloride, and recrystallised from ethanol to give *phenyl* N-p-*tolylbenzimidate* (50 g.), needles, m. p. 117—119° (Found: C, 83·7; H, 6·1. $C_{20}H_{17}ON$ requires C, 83·6; H, 5·9%). This (30 g.) was heated at 290° for 2 hr. On cooling, a dark brown glass was obtained which could not be crystallised. The crude *N*-benzoyl-4-methyldiphenylamine was therefore dissolved in ethanol (100 ml.) and refluxed for 2 hr. with potassium hydroxide (30 g.) in water (30 ml.). The ethanol was distilled off, and the residue diluted with water and extracted with chloroform whose removal from the dried (Na_2SO_4) extract left a brown solid which crystallised from aqueous ethanol (charcoal) to give 4-methyldiphenylamine (16 g.), colourless needles, m. p. 88° (Ullmann [10] recorded m. p. 89°).

N-o-*Aminobenzoyl*-4-*methyldiphenylamine.*—As described for *N*-*o*-nitrobenzoyldiphenylamine, 4-methyldiphenylamine (8 g.) and *o*-nitrobenzoyl chloride (9 g.) in presence of pyridine (10 ml.) and ether (50 ml.) gave 4-*methyl*-N-o-*nitrobenzoyldiphenylamine* (12 g.), pale yellow needles, m. p. 140°, from ethanol (Found: C, 71·9; H, 5·0. $C_{20}H_{16}O_3N_2$ requires C, 72·3; H, 4·8%). This (8 g.) in benzene (150 ml.) with Raney nickel (8 g.) was shaken with hydrogen at atmospheric pressure until the required volume had been absorbed. The Raney nickel was filtered off, and the solution concentrated. The white residue gave N-o-*aminobenzoyl*-4-*methyldiphenylamine* (7·0 g.), needles, m. p. 134—135°, from ethanol (Found; C, 78·9; H, 6·1. $C_{20}H_{18}ON_2$ requires C, 79·4; H, 6·0%).

9-p-*Tolyloxyphenanthridine.*—9-Chlorophenanthridine (2 g.) was heated with *p*-cresol (10 g.) at 160° for 2 hr. Sodium hydroxide solution was added and the mixture extracted with chloroform whose removal from the dried (Na_2SO_4) extract left a yellow solid which, recrystallised from ethanol, gave 9-p-*tolyloxyphenanthridine* (2·2 g.), needles, m. p. 117° (Found: C, 84·0; H, 5·2. $C_{20}H_{15}ON$ requires C, 84·2; H, 5·3%).

10-p-*Tolylphenanthridone.*—9-*p*-Tolyloxyphenanthridine (1 g.) was heated at 360° for 2 hr. Recrystallisation of the resultant dark brown solid from ethanol (charcoal) gave 10-p-*tolylphenanthridone* (0·7 g.), needles, m. p. 184—186° (Found: C, 84·3; H, 5·5%).

[10] Ullmann, *Annalen*, 1907, **355**, 325.

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Thermal Decomposition in Aqueous Solution of the Diazonium Chloride from N-o-*Aminobenzoyl*-4-*methyldiphenylamine.*—The amine (2·7 g.), suspended in hydrochloric acid (15 ml.) and water (30 ml.), was diazotised with sodium nitrite (0·7 g.) in water (10 ml.) Urea (0·5 g.) was added and the solution diluted to 200 ml. and warmed to 80° for 1 hr. A brown oil separated. The extract with chloroform was dried (Na_2SO_4) and concentrated. The residual brown gum was washed, with benzene (3 × 15 ml.), leaving a white solid which crystallised from ethanol in plates (0·10 g.), m. p. 218—223° (Found: C, 79·0; H, 5·5%). The benzene solution was adsorbed on alumina (100 g.). Elution with benzene–light petroleum (1 : 1) (300 ml.) gave a small amount of a yellow gum. Benzene–light petroleum (2 : 1) (500 ml.) gave 10-*p*-tolylphenanthridone (0·17 g.), needles, m. p. 184—185°, from light petroleum, identical with the compound obtained as above from 9-*p*-tolyloxyphenanthridine. Further elution with benzene–light petroleum, benzene, and benzene–ether gave a yellow gum which melted over a wide range. Ether and methanol gave a brown tar (0·5 g.). The gum was heated with 100% phosphoric acid (15 g.) at 150° for 2 hr. Water was added, and the mixture extracted with chloroform, whose removal left a dark brown tar which, on extraction with hot benzene, left a black tar which could not be crystallised. The benzene extract was adsorbed on alumina (80 g.). Elution with benzene–light petroleum (1 : 10) (300 ml.) gave a trace of pale green gum. Benzene–light petroleum (1 : 1) (300 ml.) gave 10-*p*-tolylphenanthridone (0·06 g.), needles, m. p. 184—185° from light petroleum. Further elution with benzene–light petroleum and benzene gave a mixture (0·56 g.), which was rechromatographed on silica gel but no pure product was obtained. Elution with ether and methanol gave brown tars.

Catalytic Decomposition of the Diazonium Chloride from N-o-*Aminobenzoyl*-4-*methyldiphenylamine.*—The amine (2 g.) was diazotised as described above and the diazonium solution diluted to 200 ml. Addition of copper powder (3 g.) caused vigorous evolution of nitrogen and after 1 hr. the solution no longer gave a positive test with alkaline β-naphthol. The mixture was filtered and both filtrate and residue were extracted with chloroform. The extract was dried (Na_2SO_4) and concentrated and the residual dark brown glass was dissolved in benzene and adsorbed on alumina (100 g.). Elution with benzene–light petroleum (2 : 1) (200 ml.) gave 10-*p*-tolylphenanthridone (0·075 g.), m. p. 184—185°. Further elution with benzene–light petroleum, benzene, and benzene–ether gave a mixture. Ether and methanol gave brown tar (0·2 g.). The mixture was heated with 100% phosphoric acid (20 g.) at 150° for 2 hr. Addition of water gave a brown oil which was extracted with chloroform. Removal of the solvent from the dried (Na_2SO_4) extract left a brown oil which was dissolved in benzene and adsorbed on alumina (80 g.). Elution with benzene–light petroleum (1 : 4) (400 ml.) gave a mixture of fluorenones which was purified by vacuum sublimation at 50—70°/10^{-3} mm. Spectroscopy [5] showed this to consist of fluorenone (0·290 g.) and 2-methylfluorenone (0·347 g.). Further elution with benzene–light petroleum (2 : 1) (400 ml.) gave 10-*p*-tolylphenanthridone (0·20 g.), m. p. 183—185°. Benzene and benzene–ether gave a mixture (0·45 g.) and ether gave a brown tar (0·08 g.): the mixture was rechromatographed but no separation was achieved.

N-o-*Aminobenzoyl*-4-*chlorodiphenylamine.*—As for *N*-*o*-nitrobenzoyldiphenylamine, 4-chlorodiphenylamine (10 g.) and *o*-nitrobenzoyl chloride (12 g.) in presence of pyridine (15 ml.) and ether (50 ml.) gave N-o-*nitrobenzoyl*-4-*chlorodiphenylamine* (11·2 g.), pale yellow needles, m. p. 112—114°, from ethanol (Found: C, 65·0; H, 4·1. $C_{19}H_{13}O_3N_2Cl$ requires C, 64·7; H, 3·8%). This (8 g.) in benzene (200 ml.) with Raney nickel (8 g.) was hydrogenated at room temperature and pressure. The Raney nickel was filtered off and the solution concentrated. The white residue gave N-o-*aminobenzoyl*-4-*chlorodiphenylamine* (7·0 g.) in needles, m. p. 163—165°, from ethanol (Found: C, 70·8; H, 4·3. $C_{19}H_{15}ON_2Cl$ requires C, 70·7; H, 4·6%).

9-p-*Chlorophenoxyphenanthridine.*—9-Chlorophenanthridine (2 g.) was heated with *p*-chlorophenol (10 g.) at 150° for 1 hr. Addition of excess of aqueous sodium hydroxide gave a white precipitate which, recrystallised from ethanol, gave 9-p-*chlorophenoxyphenanthridine* (2·6 g.), needles, m. p. 151—152° (Found: C, 74·5; H, 4·2. $C_{19}H_{12}ONCl$ requires C, 74·6; H, 3·9%).

10-p-*Chlorophenylphenanthridone.*—9-p-Chlorophenoxyphenanthridine (1 g.) was heated at 350° for 2 hr. The resulting dark brown solid, on recrystallisation from ethanol (charcoal), gave 10-p-*chlorophenylphenanthridone* (0·75 g.), plates, m. p. 251—252° (Found: C, 74·5; H, 4·2. $C_{19}H_{12}ONCl$ requires C, 74·6; H, 3·9%).

Thermal Decomposition in Aqueous Solution of the Diazonium Sulphate from N-o-*Aminobenzoyl*-4-*chlorodiphenylamine.*—Sodium nitrite (1 g.) was added slowly with stirring to concentrated sulphuric acid (15 ml.). This solution was cooled to 5° and a cold solution of the amine

(2·5 g.) in acetic acid (15 ml.) was added dropwise, and the mixture stirred at 5° for 2 hr. The mixture was poured on ice (400 g.), and the solution filtered to remove unchanged amine (0·25 g.) and then warmed to 80° for 1 hr. A brown tar separated. This was extracted with chloroform, and the extract dried (Na_2SO_4) and concentrated to give a brown solid, which was dissolved in benzene (30 ml.) and adsorbed on an alumina column (100 g.). Elution with benzene–light petroleum (2 : 1) (300 ml.) gave a little pale green gum. Benzene (600 ml.) gave 10-*p*-chlorophenylphenanthridone (0·51 g.), plates, m. p. 251—252°, from ethanol, identical with the authentic specimen. Further elution with benzene (800 ml.) gave 3-*chloro*-10-*phenylphenanthridone* (0·20 g.), prisms, m. p. 211—212°, from ethanol (Found: C, 74·55; H, 3·9. $C_{19}H_{12}ONCl$ requires C, 74·6; H, 3·9%). Elution with benzene and benzene–ether gave a mixture (0·60 g.). Ether gave a green oil (0·05 g.), and methanol a red-brown tar (0·35 g.). The mixture was heated with phosphoric acid (15 g.) at 150° for 2 hr. Water was added, and a dark brown tar precipitated. This was extracted with chloroform; part was insoluble and was also insoluble in benzene and ethanol, and could not be crystallised. The chloroform solution was dried (Na_2SO_4), and the solvent removed. The residual brown tar was dissolved in benzene and adsorbed on an alumina column (80 g.). Elution with benzene (700 ml.) gave 3-chloro-10-phenylphenanthridone (0·06 g.), m. p. 211—212°. Further elution with benzene and benzene–ether gave a mixture (0·05 g.). Ether and methanol gave a brown tar (0·16 g.).

Catalytic Decomposition of the Diazonium Chloride from N-o-*Aminobenzoyl*-4-*chlorodiphenylamine.*—The amine (4·0 g.), suspended in hydrochloric acid (20 ml.) and water (40 ml.), was diazotised with sodium nitrite (1·2 g.) in water (10 ml.). After being stirred for 1 hr. the mixture was diluted to 250 ml., and unchanged amine (1·6 g.) filtered off. Copper powder (3 g.) was added, and the solution stirred for 2 hr. until it no longer gave a positive test with alkaline β-naphthol. The mixture was filtered and both filtrate and residue were extracted with chloroform. The chloroform was removed from the dried (Na_2SO_4) extract, and the residual yellow gum dissolved in benzene and adsorbed on alumina (100 g.). Elution with benzene (500 ml.) gave 10-*p*-chlorophenylphenanthridone (0·38 g.), plates, m. p. 250—252°, from benzene. Benzene (800 ml.) gave 3-chloro-10-phenylphenanthridone (0·30 g.), prisms, m. p. 211—212°, from ethanol. Further elution with benzene and benzene–ether (1 : 1) gave a mixture (1·23 g.). Ether gave a yellow gum (0·09 g.) and methanol gave a red tar (0·12 g.). The mixture was heated with phosphoric acid (15 g.) at 150° for 2 hr. Water was added, and the mixture extracted with chloroform. The extract was dried (Na_2SO_4) and concentrated, and the residue dissolved in benzene and adsorbed on alumina (80 g.). Elution with benzene–light petroleum (1 : 1) (400 ml.) gave a mixture of fluorenones. This was purified by vacuum sublimation at 50—80°/10^{-3} mm. Spectroscopy [5] showed it to consist of fluorenone (0·273 g.) and 2-chlorofluorenone (0·298 g.). Elution with benzene and benzene–ether gave 3-chloro-10-phenylphenanthridone (0·13 g.), m. p. 211—212°. Ether and methanol gave a little yellow gum.

4-*Methyldiphenyl*-2′-*carboxyanilide.*—4-Methyldiphenyl-2′-carboxylic acid (0·4 g.), prepared as described above, in dry benzene (30 ml.) and thionyl chloride (5 ml.) were refluxed for 30 min. About half the solvent was distilled off, more benzene (50 ml.) was added, and again about half the solvent distilled off. Aniline (1 g.) was added, and the mixture refluxed for 30 min. The solution was washed with dilute aqueous acid, and alkali, and dried (Na_2SO_4). The residue, after removal of the solvent, was recrystallised from aqueous ethanol to give 4-*methyldiphenyl*-2′-*carboxyanilide* (0·42 g.), needles, m. p. 150—152° (Found: C, 83·0; H, 5·8 $C_{20}H_{17}ON$ requires C, 83·6; H, 6·0%). Similarly prepared from 0·4 g. of acid and 1 g. of amine were *diphenyl*-2-*carboxy*-p-*toluidide* (0·5 g.), needles, m. p. 143—145° from aqueous ethanol (Found: C, 83·3; H, 5·7%), *diphenyl*-2-*carboxy*-p-*chloroanilide* (0·45 g.), plates, m. p. 165—167°, from ethanol (Found: C, 73·9; H, 4·6. $C_{19}H_{14}ONCl$ requires C, 74·15; H, 4·5%), and (from 4-chlorodiphenyl-2′-carboxylic acid [11]) 4-*chlorodiphenyl*-2′-*carboxyanilide* (0·45 g.), needles, m. p. 196—198°, from ethanol (Found: C, 74·6; H, 4·4%).

Conversion of Anilides into Fluorenones.—Each of the four anilides (*ca.* 0·3 g.) was heated with 100% phosphoric acid (10 g.) at 150° for 2 hr. The product was diluted with water and extracted with chloroform. The dried (Na_2SO_4) extract was concentrated, and the residue purified by vacuum sublimation at 50—80°/10^{-3} mm. to give the corresponding fluorenones. Thus diphenyl-2-carboxy-*p*-toluidide (0·2965 g.) gave fluorenone (0·180 g.), m. p. and mixed m. p. 83°; 4-methyldiphenyl-2′-carboxyanilide (0·301 g.) gave 2-methylfluorenone (0·193 g.), m. p. 92°; diphenyl-2-carboxy-*p*-chloroanilide (0·300 g.) gave fluorenone (0·171 g.), m. p. and

[11] Heilbron, Hey, and Wilkinson, *J.*, 1938, 113.

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mixed m. p. 83°; 4-chlorodiphenyl-2'-carboxyanilide (0·305 g.) gave 2-chlorofluorenone (0·208 g.), m. p. and mixed m. p. 123°.

4-*Methoxycarbonyldiphenylamine*.—Methyl *p*-hydroxybenzoate (45 g.) was added to a cold solution of sodium (6·2 g.) in anhydrous ethanol (250 ml.). When solution was complete, *N*-phenylbenzimidoyl chloride in dry ether (250 ml.) was added. [The benzimidoyl chloride was prepared by heating benzanilide (48 g.) and phosphorus pentachloride (52 g.) at 100° until no more hydrogen chloride was evolved, and then distilling off phosphorus oxychloride under reduced pressure.] The mixture was allowed to stand overnight, then the precipitated sodium chloride was filtered off. The filtrate was evaporated to dryness, and crystallisation of the residue from ethanol gave p-*methoxycarbonylphenyl N-phenylbenzimidate* (59 g.), needles, m. p. 108—109° (Found: C, 75·6; H, 5·1. $C_{21}H_{17}O_3N$ requires C, 76·1; H, 5·1%). The benzimidate (50 g.) was heated at 300° for 2 hr. Crystallisation of the product from ethanol (charcoal) gave *N-benzoyl*-p-*methoxycarbonyldiphenylamine* (42 g.), prisms, m. p. 112—114° (Found: C, 76·5; H, 5·0. $C_{21}H_{17}O_3N$ requires C, 76·1; H, 5·1%). The benzoyl derivative (35 g.) in ethanol (100 ml.) was refluxed for 2 hr. with potassium hydroxide (50 g.) in water (50 ml.). Most of the ethanol was distilled off and the free acid was precipitated with hydrochloric acid, filtered off, and washed with hot water (3 × 50 ml.). Recrystallisation from benzene gave *diphenylamine-4-carboxylic acid* (16·5 g.), plates, m. p. 156—157° (Found: C, 72·8; H, 5·1. $C_{13}H_{11}O_2N$ requires C, 73·2; H, 5·2%). Dry hydrogen chloride was passed into a solution of the acid (7 g.) in anhydrous methanol (50 ml.) until the solution was saturated. After being boiled under reflux for 2 hr. the solvent was distilled off, and the residue dissolved in ether. The ethereal solution was washed with aqueous sodium carbonate and with water and dried (Na_2SO_4). Removal of the solvent left a brown solid which, on crystallisation from ethanol, gave 4-*methoxycarbonyldiphenylamine* (6·2 g.), needles, m. p. 115—117° (Found: C, 73·8; H, 5·6. $C_{14}H_{13}O_2N$ requires C, 74·0; H, 5·7%). Neither the acid nor its methyl ester could be converted into the *o*-nitrobenzoyl derivative by reaction with *o*-nitrobenzoyl chloride.

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302. *The Electronic Spectrum of the Nitrate Ion and Related Molecules.*

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The absorption spectrum of crystalline sodium nitrate has been measured in polarized ultraviolet light. Assigments are given for the two prominent absorption bands.

ALTHOUGH some discussion of the one-electron orbitals of the nitrate ion [1,2] and some determinations [3] of the crystal spectrum of sodium nitrate at room temperature have been reported, we know of no previous consideration of the electronic states in the light of the polarized spectra. This we now give, together with the ultraviolet spectrum of a sodium nitrate single crystal at −186° taken with a continuum of plane-polarized light.

EXPERIMENTAL

The solution spectrum of sodium nitrate was recorded with a " Unicam " S.P. 500 spectrophotometer.

The crystal spectra were obtained on single crystals prepared by melting sodium nitrate between silica discs so that the least possible decomposition occurred. The crystals used were

[1] Mulliken, *Phys. Rev.*, 1933, **43**, 279.
[2] Walsh, *J.*, 1953, 2301.
[3] Krishnan and Dasgupta, *Nature*, 1930, **126**, 12.

2—4 μ thick, from measurements with an Ehringhaus compensator. They were illuminated with a continuum of plane-polarized light obtained from a hydrogen lamp and polarized by passage through a Wollaston prism which could be rotated through 180° to interchange the two beams. The spectra were recorded photographically, and microphotometer tracings prepared from the plates.

Results

The spectrum of sodium nitrate in aqueous solution shows evidence of two main transitions. The first, for which $\varepsilon_{max.} = 7{\cdot}3$, and the beginning of the second, were measured, and are shown in Fig. 1. The extinction coefficient at the 2000 Å maximum was measured by Scheibe [5] as 10,000. Microphotometer tracings of sample crystal spectra are also shown in Fig. 1.

There is a close resemblance between the solution and the crystal spectra, although the position of maximum absorption is shifted from 3020 Å in water to 2870 Å in the stronger crystal spectrum.

The value of $\varepsilon_{max.}$ measured on one crystal spectrum was *ca.* 30 for " parallel " orientation. This corresponds to a value of 10 for random orientation of the absorbing ions, as obtains in solution. This figure is in fair agreement with the experimental $\varepsilon_{max.}$ in solution.

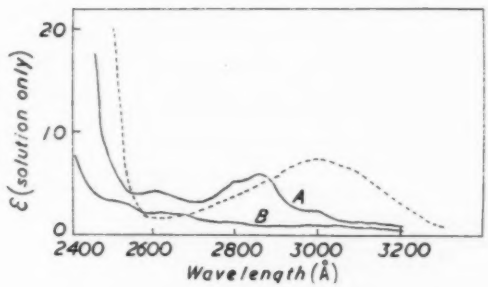

FIG. 1. *Absorption spectra of sodium nitrate solution at* 20° (– – – –) *and crystal at* −186° (——). *The two crystal spectra shown are for light polarized parallel* (*A*) *and perpendicular* (*B*) *to the planes containing the* NO_3^- *ions.*

The crystal structure [4] of sodium nitrate is especially well suited to experiments with polarized light since all the nitrate ions lie with their planes parallel. Our results, in agreement with earlier ones,[3] show that absorption is greater when the electric vector of the light vibrates parallel to the plane of the nitrate ion. It was thought that lowering the temperature to −186° might result in the appearance of some vibrational structure in the bands which at room temperature show none. Only the merest beginnings of structure were in fact apparent. There are some badly defined shoulders on some of the curves at 3010, 2970, and 2935 Å (max.). It is possible that a much lower temperature would reveal more structure but the photodissociation of the nitrate ion is unlikely to allow anything like the well-resolved nitrite-ion spectrum [6] to be obtained.

The orbital description of polyatomic molecules and ions was largely developed by Mulliken.[1] Later, Walsh discussed [2] the orbitals which occur in systems with 24 valence electrons, *e.g.*, CO_3^{2-}, NO_3^-, BF_3, and SO_3, all of which are planar in the ground state and should resemble each other spectroscopically. The orbital description given here differs from that of Walsh in that the bonding orbitals of the oxygen atoms are considered to be *sp* hybrids, with the consequence that each oxygen atom has its second lone-pair also in an *sp* hybrid orbital instead of in a pure *s* orbital. This we consider to be slightly nearer to reality, in view of the nearly similar " radii " of the 2*s* and 2*p* atomic orbitals of oxygen. The final theoretical description will need a full study of configurational interaction.

[4] Wyckoff, *Phys. Rev.*, 1920, **16**, 149.
[5] Scheibe, quoted by Rabinowitch, *Rev. Modern Phys.*, 1942, **14**, 121.
[6] Sidman, *J. Amer. Chem. Soc.*, 1957, **79**, 2669.

The sixteen molecular orbitals constructed from the atomic orbitals with $n = 2$ can be arranged in five groups, *viz.*: σ, n_h, n_p, π, and σ^*. The three σ orbitals bond nitrogen to oxygen and are built from a trigonal hybrid orbital on nitrogen and a digonal hybrid on oxygen. The σ^* antibonding orbitals are built from similar orbitals out-of-phase. Non-bonding orbitals on oxygen are denoted by n_h or n_p and consist either of sp hybrid, h orbitals or else p orbitals with axes in-plane and perpendicular to the N–O bond. Four orbitals with a nodal plane in the plane of the nitrate ion can be built from p orbitals on N and O which have axes perpendicular to the plane of the ion. Of all the orbitals, σ orbitals are assumed to have the greatest ionization potential and σ^* the least. Neither type is needed for our interpretation of the nitrate spectrum.

Regarded as molecular orbitals, all types σ, n, and π can be given a symmetry description in the group [7] D_{3h}. Thus, n (sp) molecular orbitals are a_1' and a'. If S, T, and U denote the hybrid orbitals on the three oxygen centres, $(1/\sqrt{3})\ (S + T + U)$ denotes an a_1' orbital and $(1/\sqrt{2})\ (S - T)$ or $(1/\sqrt{2})\ (T - U)$ denotes an e' orbital. It follows that

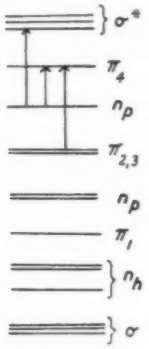

FIG. 2. *Energy levels (schematic) of the nitrate ion.*

the a_1' orbital is the more bonding of the two and will, therefore, have the greater ionization potential. The sequence in energy of the remainder of the orbitals has been given by Walsh and so the ground state can be described, with neglect of crystal perturbation, as

$$(\sigma)^6\ (n_h, a_1')^2(n_h, e')^4(\pi_1, a_2'')^2(n_p, e')^4(\pi_{2,3}, e'')^4(n_p, a_2)^2 : A_1'$$

The lowest unoccupied orbital is (π_4, a_2'') and above it lie the σ^* orbitals of which the lowest is (σ^*, a_1'). The sequence of energies is shown in Fig. 2.

Various excited states are possible. Those of lowest energy are likely to be:

$$\ldots\ldots(\pi_{2,3}, e'')^4\ (n_p, a_2')\ (\pi_4, a_2'') : A_1''$$
$$\ldots\ldots(\pi_{2,3}, e'')^4\ (n_p, a_2')(\pi_4, a_2'') : E'$$
$$\ldots\ldots(\pi_{2,3}, e'')^4\ (n_p, a_2')\ (\sigma^*, a_1) : A_2'$$

In each case singlet and triplet levels are possible but we assume that there is no need at present to discuss the triplet levels.

Pure electronic transitions from the ground state to the A_1'' and A_2' upper states are forbidden, but that to the E' state is allowed in xy polarization, where x and y are directions in the plane of the ion. Consideration of the observed extinction coefficients suggests that the long-wavelength transition could be electronically forbidden but that the transition at 2000 Å in solution might well be allowed. An interpretation of the 2000 Å transition as

[7] The group theory nomenclature is that of Eyring, Walter, and Kimball, "Quantum Chemistry," John Wiley and Sons, New York, 1943.

$E' \leftarrow A_1'$ is there indicated. The observed polarization agrees with this assignment, although no (0–0) band has been identified. In considering the absorption at longer wavelengths McConnell has suggested [8] on the basis of a study of solvent effects on the solution spectra that a $\pi \leftarrow n$ transition is present. Such a transition is electronically forbidden. It may therefore be described as $A_1'' \leftarrow A_1'$. In order to account for the observed (xy) polarization an out-of-plane ε'' vibration must be assumed to be present. This is quite possible. The observed intensity would then be the result of "stealing" from the neighbouring $E' \leftarrow A_1'$ transition (cf. the spectrum of benzene, where a similar phenomenon occurs).

The spectrum of SO_3 is found in a similar region to that of NO_3^-, but the extinction coefficient is [9] considerably smaller, being only 100 at 2000 Å. For this reason Walsh [2] assumed that there were two forbidden transitions in this region, and associated them with the A_1'' and A_2' upper states. The transition to the E' state of SO_3, then, must occur below 2000 Å. It is possible that the $A_2' \leftarrow A_1'$ transition is present also in the NO_3^- spectrum, buried beneath other absorption.

The lack of structure in the low-temperature spectrum remains to be discussed. This can be attributed to predissociation. Occupancy of the π_4 orbital is expected [2] to confer anti-bonding character upon the N–O bond. In addition the occurrence of the maximum intensity in the long-wave band at a considerable distance, over 300 Å, from the (0–0) band indicates that the excited state has an equilibrium configuration very different from the ground state. The excited A_1'' state is expected to be pyramidal and the vibrations present in the transition are therefore expected to be out-of-plane motions which carry the planar configuration into the pyramidal. The vibrational interval thought to be present (*ca.* 400 cm.$^{-1}$) is therefore partially identified. There is a similar interval of 430 cm.$^{-1}$ in the SO_3 spectrum.

Nitrites absorb at longer wavelengths than nitrates. The long-wavelength transition in nitrites has been assigned [10] to a $\pi \leftarrow n_N$ transition, where n_N denotes a non-bonding orbital on the nitrogen centre. Such a transition is impossible with nitrates. Its absence is therefore indirect evidence which confirms the nitrite-ion assignment. The occurrence of absorption near 3100 Å in NO_2Cl, HNO_3, and nitro-alkanes as well as in nitrates and in alkaline nitrite solution was associated by Trawick and Eberhardt with a $\pi \leftarrow n_O$ transition, where the n_O refers to an oxygen orbital. This assignment was made on the basis of a consideration of intensity of absorption and is seen to be consistent with the fuller orbital descriptions now given.

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[*Received, December 10th*, 1958.]

[8] McConnell, *J. Chem. Phys.*, 1952, **20**, 700.
[9] Fajans and Goodeve, *Trans. Faraday Soc.*, 1937, **33**, 614.
[10] Trawick and Eberhardt, *J. Chem. Phys.*, 1954, **22**, 1462.

303. *Physicochemical Studies of Some Cyclic Carbonates. Part II.* The Rates of Hydrolysis of Ethylene Carbonate and of Propylene Carbonate.*

By R. Kempa and W. H. Lee.

The kinetics of the hydrolyses of ethylene carbonate and propylene (*i.e.*, methylethylene) carbonate, in alkaline aqueous media, at 25° have been studied; rate constants, k_{OH}, are 48·8 and 17·8 l. mole^{-1} min.$^{-1}$, respectively. Conductimetry was used to study the initial rates of the water-catalysed hydrolyses of these two compounds; at 25°, the initial rate constants k_{H_2O} were $14{\cdot}2 \times 10^{-7}$ and $7{\cdot}1 \times 10^{-7}$ min.$^{-1}$, respectively. At 18°, k_{H_2O} for ethylene carbonate was $5{\cdot}7 \times 10^{-7}$ min.$^{-1}$, leading to an activation energy for its initial hydrolysis of 22·5 kcal./mole.

Ethylene carbonate for use in cryoscopy was reported to be non-hygroscopic, and no precautions were taken to prevent the absorption of moisture from the air.[1] We have found, however, that the conductivity of samples of carefully purified cyclic carbonates, left in stoppered conductivity cells in a thermostat, progressively increases. The effect appeared to be due to hydrolysis; as it is intended to carry out reactions in water, and in aqueous solutions, in order to study complex-formation of metal ions by cyclic carbonates, it seemed of interest to obtain rates of hydrolysis of ethylene carbonate and of propylene carbonate, in aqueous alkaline solution and in water.

Alkaline Hydrolysis.—Alkaline hydrolyses were followed by titration, as in Skrabal and Baltadschiewa's studies of open-chain esters.[2] The rates were so much greater than those for hydrolysis by water molecules that we may write for the rate equation in alkaline solution:

$$dx/dt = k_{OH}[OH^-][C_2H_4CO_3] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where k_{OH} is the rate constant, $[C_2H_4CO_3]$ is the concentration of ethylene carbonate, and x is the amount of ethylene carbonate hydrolysed; an analogous equation applies for propylene carbonate. The reaction $C_2H_4CO_3 + OH^- + H_2O \longrightarrow (CH_2{\cdot}OH)_2 + HCO_3^-$ proceeds rapidly even in very dilute solutions of caustic alkalis, and it was convenient to study the rate of hydrolysis in sodium carbonate solution. From the hydrolysis: $CO_3^{2-} + H_2O \rightleftharpoons OH^- + HCO_3^-$, of hydrolysis constant K', we can express the hydroxyl-ion concentration as

$$[OH^-] = K'[CO_3^{2-}]/[HCO_3^-] \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

so that eqn. (1) becomes

$$dx/dt = k[C_2H_4CO_3][CO_3^{2-}]/[HCO_3^-] \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where $k = k_{OH} \times K'$. If the initial concentrations of cyclic carbonate and of alkali carbonate are equal, eqn. (3) becomes $dx/dt = k(a - x)^2/x$, where a is the initial concentration, and x the amount of ester hydrolysed. The extent of reaction can thus be determined from the change in carbonate ion–bicarbonate ion ratio with time, as found by titration.

Integration of this special form of the rate equation gives:

$$k = \frac{1}{t}\left[\frac{a}{a-x} - 1 - \ln\frac{a}{a-x}\right] = \frac{Z}{t}$$

and k can be obtained from the graph of Z against time t. To obtain the rate constant k_{OH} from k, we have for the second dissociation of carbonic acid:

$$K_2 = \frac{[CO_3^{2-}][H^+]}{[HCO_3^-]} = \frac{[CO_3^{2-}]K_w}{[HCO_3^-][OH^-]}$$

* *J.*, 1958, 1936, is considered as Part I.

[1] Gross and Schuerch, *Analyt. Chem.*, 1956, **28**, 227.

[2] Skrabal and Baltadschiewa, *Monatsh.*, 1924, **45**, 95.

By comparison with eqn. (2), $K' = K_w/K_2$, and hence $k_{OH} = kK_2/K_w$. In the derivation of k_{OH}, the following values were taken, for 25°:

$$K_2 = 4{\cdot}69 \times 10^{-11}; \quad K_w = 1{\cdot}008 \times 10^{-14}$$

The results for the alkaline hydrolyses of ethylene carbonate and propylene carbonate are given in Tables 1 and 2; values of Z/t are listed, but k and k_{OH} were obtained from the slope of the best straight line for Z plotted against time.

TABLE 1. *Alkaline hydrolysis of ethylene carbonate at* 25°.

No.	t (min.)	$(a-x)$ (mole l.$^{-1}$)	Z	$10Z/t$	No.	t (min.)	$(a-x)$ (mole l.$^{-1}$)	Z	$10Z/t$
		Expt. 1.					Expt. 2.		
1	0	0·03692	0	—	1	0	0·01698	0	—
2	11	0·02473	0·130	0·118	2	5	0·01291	0·041	0·082
3	25	0·02124	0·242	0·097	3	10	0·01087	0·116	0·116
4	55	0·01617	0·555	0·101	4	15	0·01019	0·156	0·104
5	70	0·01506	0·664	0·095	5	30	0·00842	0·315	0·105
6	95	0·01284	0·959	0·101	6	50	0·00734	0·475	0·095
7	125	0·01141	1·23	0·098	7	70	0·00598	0·796	0·114
8	160	0·00951	1·73	0·108	8	90	0·00557	0·934	0·104
					9	120	0·00475	1·30	0·108
					10	150	0·00421	1·64	0·109
					11	240	0·00353	2·24	0·093

$k = 1{\cdot}05 \times 10^{-2}$; $k_{OH} = 48{\cdot}8$ l. mole^{-1} min.$^{-1}$.

TABLE 2. *Alkaline hydrolysis of propylene carbonate at* 25°.

No.	t (min.)	$(a-x)$ (mole l.$^{-1}$)	Z	$10Z/t$	No.	t (min.)	$(a-x)$ (mole l.$^{-1}$)	Z	$10Z/t$
		Expt. 1.					Expt. 2.		
1	0	0·08333	0	—	1	0	0·02315	0	—
2	5	0·06867	0·020	0·040	2	5	0·01875	0·024	0·048
3	10	0·06134	0·052	0·052	3	10	0·01693	0·051	0·051
4	15	0·05902	0·067	0·0404	4	20	0·01554	0·091	0·0455
5	25	0·05401	0·109	0·0436	5	40	0·01361	0·166	0·0415
6	40	0·05092	0·144	0·0360	6	80	0·01146	0·317	0·0396
7	70	0·04359	0·264	0·0377	7	90	0·01103	0·357	0·0397
8	90	0·03973	0·357	0·0396	8	110	0·01039	0·426	0·0387
9	120	0·03665	0·452	0·0377	9	180	0·00825	0·774	0·043

$k = 3{\cdot}87 \times 10^{-3}$; $k_{OH} = 17{\cdot}8$ l. mole^{-1} min.$^{-1}$.

Water Hydrolysis.—The rate of water-catalysed hydrolysis of open-chain esters was found by Skrabal and Baltadschiewa [2] to be immeasurably small. In the present case, it was possible to follow the initial rate by the change in electrical conductivity. It is realised that this is a very sensitive method, and that impurity of the cyclic carbonate would invalidate the results; nevertheless, from the reproducibility of conductivity of the liquid carbonate, and of the hydrolysis constant for different samples, we consider that it is essentially the hydrolysis of carbonate which is being followed.

In the case of ethylene carbonate, the water hydrolysis may be represented as $C_2H_4CO_3 + 2H_2O \longrightarrow (CH_2{\cdot}OH)_2 + H_2CO_3$. Dissociation of the carbonic acid yields an electrolyte system containing hydrogen, hydroxyl, and bicarbonate ions. Since the first dissociation constant for carbonic acid is given by $pK_1 = 6{\cdot}352$, compared with $pK_2 = 10{\cdot}329$,[3] we may neglect the second stage of dissociation, and write:

$$x = [HCO_3^-] + [H_2CO_3] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where x is the amount of ethylene carbonate hydrolysed. The specific conductivity κ may be equated, in the usual way, to the sum of the ionic mobilities:

$$1000\kappa = c(l_{H^+} + l_{HCO_3^-}) = c\Lambda_x \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

[3] Robinson and Stokes, "Electrolyte Solutions," Butterworths, London, 1955, p. 496.

Λ_x, the equivalent conductivity of the solution corresponding to an amount of hydrolysis x, differs from the sum of the ionic mobilities in aqueous solution of these ions, because of the cyclic carbonate which is present. If the validity of Walden's rule is assumed, the sum of the limiting mobilities can be corrected for the measured viscosity of the solution to give Λ_x. If K_1 is the first dissociation constant for carbonic acid, eqn. (4) is: $x = [H^+] + [H^+]^2/K_1$, and as $[H^+] = c$, obtained from eqn. (5), x can be obtained. From the variation in c, and hence of x, with time, the values of dx/dt listed in Table 3, at different initial concentrations of ethylene carbonate [$C_2H_4CO_3$], were obtained. The concentrations of hydrogen and bicarbonate ions originally present in the conductivity water can be obtained from its conductivity, and allowed for.

TABLE 3. *Initial rates of hydrolysis by water.*

a) Ethylene carbonate.

Expt.	Temp.	Λ_x	$10^8 dx/dt$	[$C_2H_4CO_3$]	$10^7 k_{OH}[OH^-]$	$10^7 k_{H_2O}$
1	25°	391·6	19·5	0·1291	1·4	13·7
2		389·9	30·3	0·1980	1·1	14·2
3		386·7	38·5	0·2452	0·9	14·8
					Average	14·2
1	18°	354·0	26·7	0·4327	0·4	5·8
2		353·8	27·3	0·4352	0·5	5·7
3		351·9	39·7	0·6620	0·4	5·6
					Average	5·7
(b) Propylene carbonate.				[$C_3H_6CO_3$]		
1	25°	392·5	16·55	0·2254	0·4	6·9
2		392·0	23·7	0·3102	0·4	7·2
3		390·5	31·05	0·3964	0·5	7·3
					Average	7·1

Allowance is made for the contribution of the alkaline hydrolysis to the rate, by calculating $k_{OH}[OH^-]$ at each initial concentration, and subtracting this from the total rate, which is $(dx/dt)(1/[C_2H_4CO_3])$.

The change in rate between 18° and 25° for ethylene carbonate corresponds to an activation energy, for the initial hydrolysis, of 22·5 kcal./mole.

Discussion.—The water-catalysed hydrolysis of ethylene carbonate at 25° is very slow, and the concentration of hydroxyl ions in conductivity water contributes about 7% of the observed total rate. The rate for propylene carbonate is almost exactly one-half of that for ethylene carbonate; the transition state in this hydrolysis is a neutral complex, so that it appears that the methyl group shields the adjacent oxygen atom from attack by a water molecule, introducing a steric probability factor of $\frac{1}{2}$ into the rate equation.

The hydroxyl-ion hydrolysis of ethylene carbonate is about three times as rapid as that of propylene carbonate; the steric factor may be increased, in this case, by the polar effect of the methyl group substituent towards alkaline hydrolysis.[4]

EXPERIMENTAL

Materials.—Ethylene carbonate and propylene carbonate were commercial samples, carefully purified as described in Part I, and having the physical properties there recorded. Conductivity water produced by ion exchange, of specific conductance *ca.* $0·5 \times 10^{-6}$ mho (determined for each sample), was used as solvent.

Procedure.—In following the alkaline hydrolyses, samples of the ester–sodium carbonate solution were withdrawn after definite intervals, cooled in an ice-bath, and titrated against hydrochloric acid of equivalent concentration to that of the sodium carbonate. Phenolphthalein was used as indicator, and titration continued to pH 8·3, as shown by comparison with a prepared buffer solution containing the same indicator.

The water hydrolyses were followed by the change in conductivity, as measured in a conductivity cell of the Hartley–Barrett type, having bright platinum electrodes; the cell was

[4] Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 758.

connected in a conventional Wheatstone bridge circuit, and a. c. power was supplied by an oscillator of frequency 1500 c./sec.

The titration technique can be used over a much wider concentration range than the conductimetric, since the use of the limiting ionic mobilities is permissible only at extreme dilution. Initial rates only are reported for the water hydrolyses; the kinetic relationship for the alkaline hydrolysis is seen to hold over at least 75% of the reaction.

BATTERSEA COLLEGE OF TECHNOLOGY, LONDON, S.W.11. [*Received, August 14th*, 1958.]

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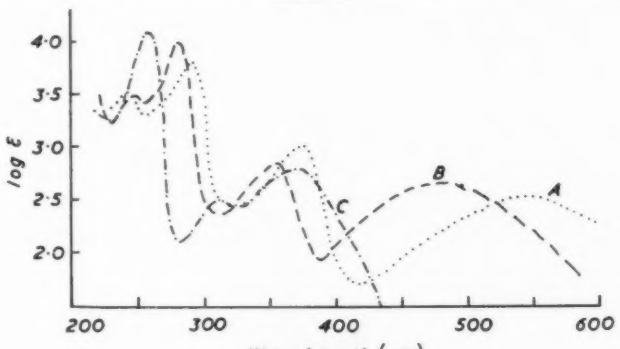
304. *Anhydro-salts. Part II.* The Absorption Spectra of Phenol-betaines.*

By J. P. SAXENA, (the late) W. H. STAFFORD, and WINIFRED L. STAFFORD.

A series of phenol-betaines has been prepared and their absorption spectra have been recorded. A marked relation between the capacity of the solvent for hydrogen-bonding and the absorption spectrum in that solvent is discussed.

THE dipolar structure of the anhydro-salt (I; R = Me) from 8-hydroxy-1-methylquinolinium hydroxide[1,2] has been confirmed by spectroscopic measurements at several pH values.[3] Its unusual colour—red as a solid, violet in non-polar solvents—merited some explanation; accordingly the betaine was prepared both by the original unusual method

FIG. 1. *8-Hydroxy-1-methylquinolinium anhydro-salt, (A) in chloroform, (B) in ethanol, (C) in acidic ethanol.*



of treating 8-hydroxyquinoline with diazomethane, and by the action of potassium carbonate on the methiodide of 8-hydroxyquinoline. The products were spectroscopically similar although analytically different owing to solvation. The observation that the compound was red in aqueous solution and purple in chloroform prompted an investigation of the influence of hydrogen-bonding on the absorption spectrum of anhydro-salts in general.

In Fig. 1, the absorption spectra of the compound (I) in chloroform, ethanol, and acid solutions are recorded. The apparent differences are attributed to the existence of the three states (I), (II), and (III) individually in the respective solvents. Comparison

* Part I, *J.*, 1952, 580.

[1] Caronna and Sansone, *Gazzetta*, 1939, **69**, 24.
[2] Schenkel-Rudin, *Helv. Chim. Acta*, 1944, **27**, 1456.
[3] Phillips and Keown, *J. Amer. Chem. Soc.*, 1951, **73**, 5483.

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of the absorption of light by the cation (III; R = Me) and by 8-hydroxyquinoline hydrochloride (cf. III; R = H) shows the expected similarity consonant with hybrid structures in which one electron pair of the phenolic group is merged with the π-electron system of the quinoline ring. In chloroform, the contributing forms (Ia, b, c, etc.) of the betaine lead to an analogous hybrid in which the structural difference that there is no sharing of an electron pair of the oxygen atom with a hydrogen atom must be responsible for the marked difference in light absorption. Coulson [4] attributes it to the fact that the bonded molecule when excited does not have enough overlap in the bonding *n*-orbital to hold it together, with the result that the excited state is of much the same energy as an unbonded molecule, whereas the energy of the ground state is lowered by that of the hydrogen bond.

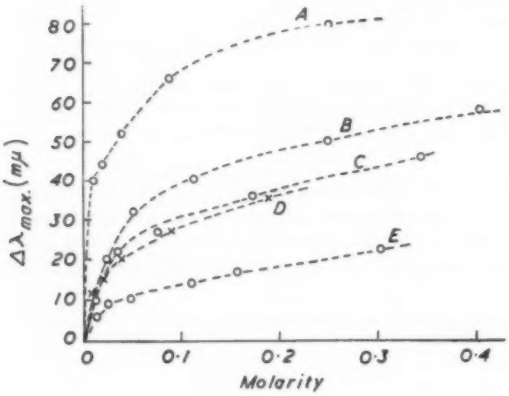
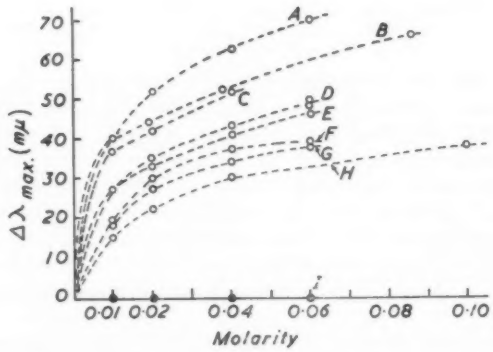


FIG. 2. *8-Hydroxy-1-methylquinolinium anhydro-salt in chloroform containing (A) 2-hydroxybiphenyl, (B) methanol, (C) ethanol, (D) borneol, (E) t-butyl alcohol.*



G. 3. *8-Hydroxy-1-methylquinolinium anhydro-salt in chloroform containing (A) p-nitrophenol, (B) 2-hydroxybiphenyl, (C) m-nitrophenol, (D) m-bromophenol, p-bromophenol, or methyl p-hydroxybenzoate, (E) m-fluorophenol, (F) p-fluorophenol, (G) methyl m-hydroxybenzoate, (H) phenol, (I) o-nitrophenol.*

The state (II) of the substance in ethanol (R′ = Et) represents an intermediate state in which an electron pair is partly shared in the hydrogen bond, mirrored in an intermediate absorption type. This large effect may be considered as due to a change in the polarisation of the molecular orbital of the quinoline ring resulting because the conjugated electron pair of the oxygen atom is progressively shared and ultimately captured by a hydrogen atom. Thus there is a displacement of the electrons in the molecular orbital resulting in the electrons' being more closely bound to the oxygen atom. In the cation (III) the forms (b), etc., contribute minimally, but in (II) and (I) they are much more important. The conclusion was reached that the deep colour of anhydro-salts of this type may be attributed to the existence of a dipolar structure in which the negative character is

[4] Coulson, *Research*, 1957, **10**, 149.

associated in part with carbon atoms of an aromatic nucleus.[5] This conclusion has been extended to explain the colour of azulene and its derivatives.[6]

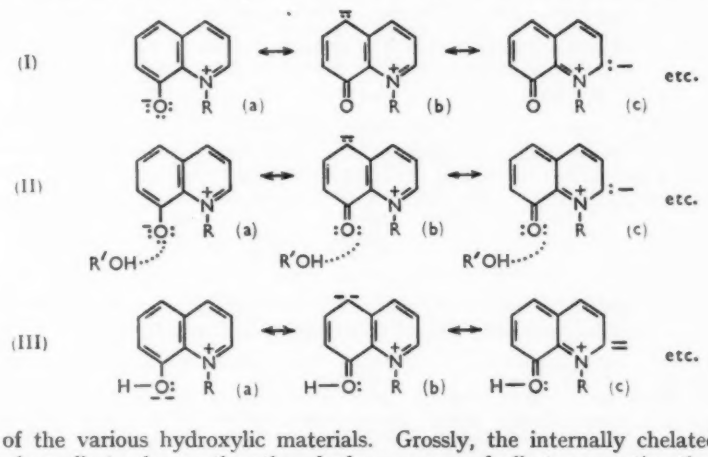
As with merocyanines, a high dielectric constant of the solvent caused hypsochromic displacements in the visible absorption maximum, shown in Table 1. The presence of

TABLE 1. *Dependence of the position of the visible absorption maximum of compound* (I) *on the dielectric constant* (ε) *of the solvent.*

Solvent	$\lambda_{max.}$ (mean)	ε at 25°	Solvent	$\lambda_{max.}$ (mean)	ε at 25°
C_6H_6	568	2·28	Bu^tOH	502	10·9
$CHCl_3$	554	4·81	EtOH	484	24·3
EtOAc	539	6·02	H_2O	443	78·5
$COMe_2$	535	20·7	$MeNO_2$	388	20·8 (or 39·4 Remick)
$PhNO_2$	530	34·8	PhOH (satd. soln.		
MeCN	512	38·8	in $CHCl_3$)	443	9·68 at 60°
o-$C_6H_4Me{\cdot}NO_2$	508	24·7			

a hydroxyl group produces a larger shift, as shown by comparing the effect of t-butyl alcohol (ε 10·9), which gives $\lambda_{max.}$ 502 mμ, with the value 535 mμ for acetone (ε 20·7). The pronounced effects of *o*-nitrotoluene and nitromethane may be attributed to their acidity, and thus also to their ability to form hydrogen bonds with the betaine.

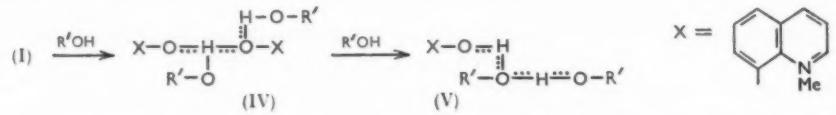
A detailed examination of the effect of hydroxylic solvents confirmed the essence of the above hypothesis, but introduced a new problem. Figs. 2 and 3 summarise a series of experiments in which the effectiveness of a number of compounds as hydrogen-bonding agents were compared (*i.e.*, R′ varied in state II). The concentration of the betaine was kept constant and the change in the visible absorption measured for different concen-



trations of the various hydroxylic materials. Grossly, the internally chelated *o*-nitrophenol had no effect, whereas the others had a pronounced effect, supporting the responsibility of hydrogen-bonding. Unexpectedly the visible absorption band moved progressively as a unit hypsochromically with no marked changes in the value of the extinction coefficient. The expectation is that an equilibrium between the two states (I) and (II) displaced by an increase in hydroxylic-solvent concentration should cause the progressive disappearance of the band corresponding to (I) and the appropriate appearance of a band corresponding to (II). In fact the maximum was translated ($\Delta\lambda_{max.}$ plotted) as the concentration of the hydroxylic solvent was increased through all intermediate positions, with no indications of an equilibrium. Figs. 2 and 3 show that the substances differ in their effect in the expected order, but the shape of the $\Delta\lambda_{max.}$–concentration

[5] Part I, Stafford, *J.*, 1952, 580.
[6] Stafford and Reid, *Chem. and Ind.*, 1954, 277.

curves is unusual. The only apparent explanation is that the first stage of the bonding is complete at the end of the sharp rise, and the subsequent slow rise is due to formation of polymeric hydrogen-bonds as in states (IV) and (V).



The translation with maintenance of the value of the extinction coefficient was not found with acetic acid. Here the normal translation occurred, but the height of the maximum diminished and the typical salt absorption appeared.

In an attempt to show the existence of hydrogen bonding between the betaine and hydroxylic solvents, Lund's work [7] on anionic systems was extended by determination of the infrared absorption spectra of solutions of the betaine in chloroform containing varying proportions of ethanol, phenol, and *p*-nitrophenol. The positions of the bands due to hydroxyl are listed in Tables 2, 3, and 4. The concentration of the betaine was constant at 0·005M while that of the hydroxylic compounds was increased over a wide range from 0·004M. The ability of these compounds to form inter-hydrogen bonds made interpretation of the spectra rather difficult but the following observations can be made.

TABLE 2. *Infrared absorption maxima in the hydroxyl region of ethanol–chloroform solutions in presence and in absence of compound* (I).

Molarity of EtOH ...	0·0041	0·0068	0·034	0·068	0·204	1·36	0·0041	1·36
Ratio, (I): EtOH ...	1 : 0·8	1 : 1·36	1 : 6·8	1 : 13·6	1 : 40·8	1 : 252	—	—
Band 1	3600s	3600s	3600s	3600ms	3590m	3580w	3630s	3620s
„ 2	3460w	3460w	3440w	3430w	3420m	3440—3260s	3460s	3480—3300s

TABLE 3. *Infrared absorption maxima in the hydroxyl region of* p-*nitrophenol–chloroform solutions in presence and in absence of substance* (I).

Molarity of *p*-NO_2·C_6H_4·OH ...	0·004	0·04	0·096	0·004	0·04	0·096
Ratio, (I): *p*-NO_2·C_6H_4·OH ...	1 : 0·8	1 : 8	1 : 19	—	—	—
Band 1	3650w	3618s	3610s	3640m	3615s	3610s
„ 2	—	3380m	3370s	—	3410m	3390s
„ 3	—	3200s	3200s	—	3207s	3220s

TABLE 4. *Infrared absorption maxima in the hydroxyl region of phenol–chloroform solutions in presence and in absence of substance* (I).

Molarity of PhOH	0·0056	0·016	0·04	0·192	0·46	0·0056	0·016	0·04	0·192	0·46
Ratio, (I): PhOH	1 : 1·1	1 : 3·2	1 : 8	1 : 38·4	1 : 92	—	—	—	—	—
Ratio, $CHCl_3$: PhOH	50 : 1	20 : 1	7·5 : 1	2 : 1	1 : 1·5	50 : 1	20 : 1	7·5 : 1	2 : 1	1 : 1·5
Band 1	3616s	3630s	3630s	3605s	3620s	3616s	3630s	3628s	3605s	3620s
„ 2	3275vw	3303w	3360, 3300 w	3325w	3570—3360s	3275vw	3303w	3400, 3355, 3320 w	3330w	3570—3360s

Both bands of ethanol solutions in chloroform are shifted to lower frequency by amounts varying from 25 to 40 cm.$^{-1}$ when the betaine is present. In addition the intensity of band 1 falls and of band 2 rises with increased ethanol concentration, indicating that the betaine reduces the concentration of free hydroxyl and increases that of bonded hydroxyl. It is noteworthy that the bathochromic shifts occur even at low betaine : ethanol ratios, suggesting that the effect is not a general one of an increasingly polar environment.

With *p*-nitrophenol, evidence again appears (Table 3) for the formation of hydrogen bonds with the betaine. The intensity of band 3 rises from that observed for the solvent, on addition of the phenol if the betaine is present, indicating that a small reduction in the

[7] Lund, *Acta Chem. Scand.*, 1958, **12**, 298.

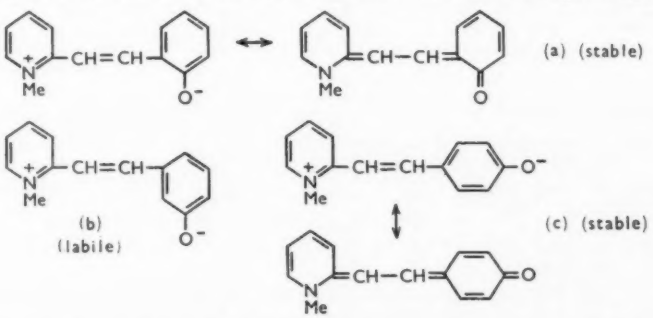
concentration of free hydroxyl and an increase in the concentration of bonded hydroxyl occur. Also band 2, due to bonded hydroxyl, is shifted to lower frequency, showing that the betaine has introduced bonds of greater strength than those present in a solvent mixture of the same proportions.

However, when phenol is used, the infrared absorption spectrum remains almost unchanged in presence or absence of the betaine. The fact that the bonded-hydroxyl band moves to higher frequency with increase of phenol concentration in contrast to the situation with the other two hydroxy-compounds examined is probably significant. The gradual shift (Table 4) from 3275 up to 3325 cm.$^{-1}$ is followed by a sharp change to a broad maximum at 3465 cm.$^{-1}$ between the chloroform : phenol ratios 2 : 1 and 1 : 1·5. This is of the same order as the findings of Bellamy, Hallam, and Williams [8] for the dilution of an acetone or acetonitrile solution of phenol with an inert solvent. Thus the complexity of the phenol–chloroform association may be preventing or masking a bonding effect to the betaine.

In Fig. 2, the curve representing the change in visible absorption maximum with concentration of ethanol shows a break from a sharp to a slow rise at about 0·04M, which, since the betaine concentration is 0·00055M, corresponds to a betaine : ethanol ratio of 1 : 70. The infrared absorption spectrum changes considerably in the bonded-hydroxyl region for solution and solvents at about this betaine : ethanol ratio, indicating the association of hydroxyl molecules as formulated for example by (V). Similarly for phenol, the change in the visible absorption curve (Fig. 3) for which a 0·001M-betaine solution was employed occurs at a betaine : phenol ratio of 1 : 10 which also corresponds to a change in the bonded-hydroxyl absorption (Table 4). In addition, the three solutions containing *p*-nitrophenol have widely different absorption in the hydroxyl region, all corresponding to different parts of the visible absorption curve. It is noteworthy that the change from a chloroform : phenol ratio of 2 : 1 to 1 : 1·5 which is strongly marked in the infrared absorption spectrum has little effect on the colour of the solution.

Since the curves showing the effect of different solvents on chloroform solutions of the betaine are almost parallel at high concentration of added material, where association of solvent molecules occurs, the influence on the visible absorption maximum of the betaine is primarily one of simple hydrogen-bonding, with the result that a convenient method is available for placing several compounds in their correct order of capacity to form external hydrogen-bonds.

The absorption spectra of anhydro-salts whose cationic and anionic centres are separated by a more extended conjugated system were examined. *o*-, *m*-, and *p*-Hydroxyphenylstilbazoles were prepared by condensing α-picoline with hydroxybenzaldehydes, and the methiodides were formed in the usual manner. Addition of aqueous potassium

(VI) 

carbonate solution to those of the *ortho*- and the *para*-isomer gave orange betaines, (VIa and c), which were extracted into chloroform as violet solutions. Only compound (VIa)

[8] Bellamy, Hallam, and Williams, *Trans. Faraday Soc.*, 1958, **54**, 1120.

was obtained crystalline. It was necessary to employ 2N-sodium hydroxide to obtain a betaine from the methiodide of the *meta*-isomer. This orange material could only sparingly be extracted into chloroform. Its lower stability is probably due to the absence of a pyridone quinone form (VIb).

The absorption maxima of *o*-, *m*-, and *p*-hydroxyphenylstilbazolium methiodide in ethanol and alkaline ethanol solution are listed in Table 5, and the spectra of the betaine (VIa) in ethanol, chloroform, and benzene are recorded in Fig. 4.

TABLE 5. *Absorption maxima of* o-, m-, *and* p-*hydroxyphenylstilbazolium methiodides.*

Isomer	$\lambda_{max.}$ (mμ)	log ε	$\lambda_{max.}$ (mμ)	log ε	$\lambda_{max.}$ (mμ)	log ε
o, in EtOH	—	—	358—360	3·98	295—299	3·96
o, in alkaline EtOH ...	494	4·36	348	4·23	250	4·12
m, in EtOH	—	—	345	4·25	276	3·84
m, in alkaline EtOH ...	425—440 (infl.)	3·6	360—362	4·22	268	3·98
p, in EtOH	—	—	372	4·16	286	4·01
p, in alkaline EtOH ...	494—496	4·44	—	—	285—286	3·84

The spectra of the betaines (VIa and c) are analogous to those of the 8-hydroxyquinolinium betaine, but with the first band bathochromically shifted and of higher extinction value, as expected for a more extended conjugated system. That of the *meta*-isomer (VIb)

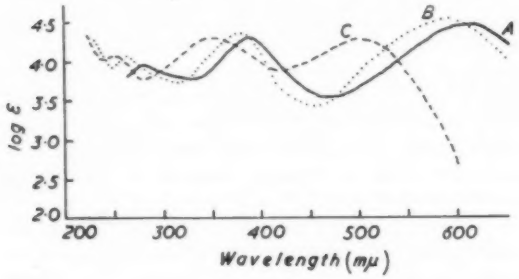


FIG. 4. (o-*Hydroxyphenyl*)-1-*methylstilbazolium anhydro-salt* (*A*) *in benzene*, (*B*) *in chloroform*, (*C*) *in ethanol.*

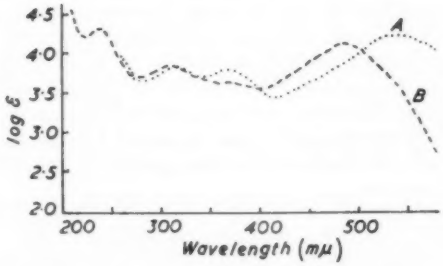


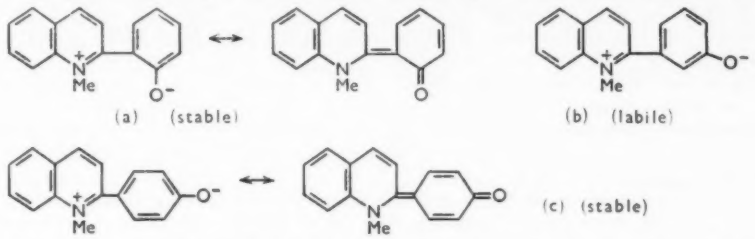
FIG. 5. 2-p-*Hydroxyphenyl*-1-*methylquinolinium anhydro-salt* (*A*) *in chloroform*, (*B*) *in ethanol.*

has a point of inflexion in place of the first peak, with extinction value comparable to that of the 8-hydroxyquinolinium anhydro-salt (Fig. 1). The hydroxyphenylstilbazolium betaines were found to be thermochromic. Thus a solution of compound (VIa) in chloroform at room temperature is purple, changing to blue at the boiling point, and to orange-red at −80°. Increase in temperature is considered to decrease the polar association of the solvent molecules with the betaine, resulting in a change analogous to state (II) ⟶ state (I).

2-*o*-, *m*-, and *p*-Hydroxyphenylquinoline were prepared by condensing *o*-aminobenzaldehyde with *o*-, *m*-, and *p*-hydroxyacetophenone, and the methiodides formed. 2-*o*-Hydroxyphenylquinolinium iodide gave no colour with alkali, probably owing to pseudo-base formation. The other two isomers yielded coloured betaines (VIIb and c), but only that from the *para*-isomer could be isolated crystalline. The absorption maxima of the

methiodides of *m*- and *p*-hydroxyphenylquinoline in ethanol and alkaline ethanol solution are given in Table 6, and the spectra of the betaine (VIIc) in ethanol and chloroform are

(VII)



recorded in Fig. 5. It is apparent that the relation between solvent and spectrum derived from the study of 8-hydroxyquinolinium anhydro-salt applies also to those with a more extended dipolar system.

TABLE 6. *Absorption maxima of* m- *and* p-*hydroxyphenylquinolinium iodide.*

Isomer	$\lambda_{max.}$ (mμ)	log ε	$\lambda_{max.}$ (mμ)	log ε	$\lambda_{max.}$ (mμ)	log ε
m, in EtOH	—	—	328—330	4·1	266—268	3·85
m, in alkaline EtOH ...	450	2·66	328—332 (infl.)	3·79	308	3·84
p, in EtOH	—	—	335—337	4·01	270	4·2
p, in alkaline EtOH ...	478—480	4·04	373	4·02	315, 282	4·11, 4·02

FIG. 6. *3-Hydroxy-1-methylpyridinium iodide (A) in ethanol, (B) in acidic ethanol, (C) in alkaline ethanol.*

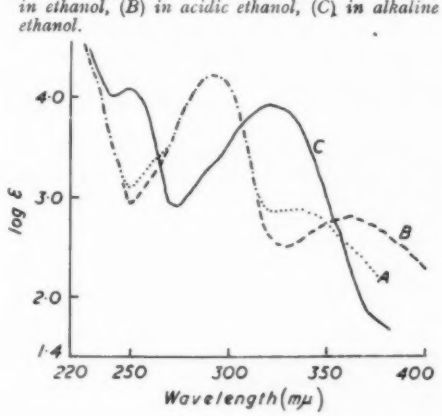
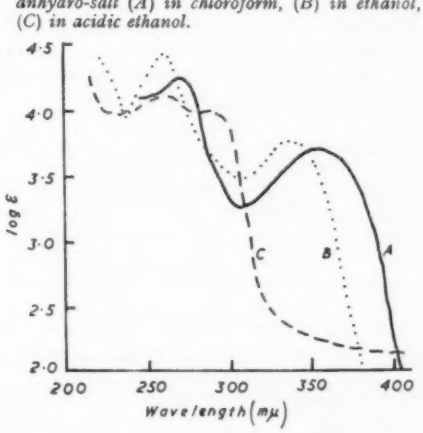
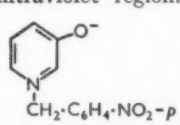


FIG. 7. *3-Hydroxy-1-p-nitrobenzylpyridinium anhydro-salt (A) in chloroform, (B) in ethanol, (C) in acidic ethanol.*



Finally, anhydro-salts from 1-alkyl-3-hydroxypyridinium hydroxides were examined to discover if the relation also holds good for those whose cationic and anionic centres are associated with a monocyclic system, and therefore whose absorption falls entirely in the ultraviolet region.[6] 3-Hydroxy-1-methylpyridinium iodide did not yield an isolable betaine on treatment with potassium carbonate solution, but its absorption spectrum was measured in acidic, ethanol, and alkaline ethanol solutions, and recorded in Fig. 6. The betaine (VIII) from 3-hydroxy-1-*p*-nitrobenzylpyridinium bromide was however obtained as a crystalline hydrate. The substance may be regarded as a pseudo-base. It yielded a picrate identical with that derived directly from the bromide. The absorption spectra in ethanol and chloroform solutions are recorded in Fig. 7. Thus the capacity of change of solvent to change the electronic state and therefore the absorption spectrum also applies to simple monocyclic anhydro-salts.



(VIII)

Experimental.

Methiodides and Derivation of Betaines.—General methods. A solution of 8-hydroxyquinoline in " AnalaR " acetone was boiled with methyl iodide for 2—3 hr., until the quaternary salt separated. The acetone and excess of methyl iodide were removed and the residue after being washed with ether was recrystallised from ethanol–ether. The methiodide was then treated with aqueous 2N-potassium carbonate, and the resulting betaine extracted into chloroform. The extract was dried (K_2CO_3) and concentrated under reduced pressure.

8-Hydroxy-1-methylquinolinium iodide had m. p. 143° (decomp.) (Found: N, 5·0; I, 44·0. Calc. for $C_{10}H_{10}ONI$: N, 4·9; I, 44·3%).

8-Hydroxy-1-methylquinolinium Anhydro-salt.—The betaine was obtained as orange crystals from the violet chloroform solution by addition of ligroin. These were converted by drying under a vacuum into violet-red needles, m. p. 115° (decomp.) (Found: C, 68·4; H, 6·16; N, 7·5. Calc. for $C_{10}H_9ON,H_2O$: C, 67·8; H, 6·2; N, 7·9%). The compound when prepared by the method of Caronna and Sansone [1] was obtained without water of crystallisation.

Preparation of Hydroxyphenylstilbazoles.—α-Picoline (10 g.), *o*- or *p*-hydroxybenzaldehyde (13 g.), and water (7 g.), in a Carius tube, were kept in an autoclave for 8 hr. at 140°. The unchanged materials were removed in steam, and the oily residue was extracted with ether. The extract was dried and evaporated. The residue was treated in ethanol solution with charcoal, and the product crystallised from ligroin, giving the *o*-, m. p. 132°, and the *p*-hydroxyisomer, m. p. 217°. *m*-Hydroxyphenylstilbazole was not formed from *m*-hydroxybenzaldehyde under these conditions. Chiang and Hartung's method [9] gave the compound obtained as colourless needles, m. p. 136°. These gave: o-*hydroxyphenyl*-1-*methylstilbazolium iodide*, m. p. 240° (Found: C, 49·0; H, 3·9; N, 3·8; I, 37·0. $C_{15}H_{14}ONI$ requires C, 49·6; H, 4·1; N, 4·1; I, 37·5%) [*picrate* (Found: N, 13·6. $C_{21}H_{16}O_8N_4$ requires N, 13·6%)]; m-*hydroxy*-1-*methylphenylstilbazolium iodide*, m. p. 205—207° (Found: C, 49·0; H, 4·4; N, 4·25; I, 37·5%); and the para-*isomer*, m. p. 257° (Found: C, 49·5; H, 4·3; N, 4·5; I, 37·0%), all yellow needles.

o-*Hydroxyphenyl*-1-*methylstilbazolium anhydro-salt* formed violet needles (from chloroform–benzene), m. p. 154° (decomp.) (Found: C, 67·0; H, 6·45; N, 5·35. $C_{14}H_{13}ON,2H_2O$ requires C, 67·9; H, 6·1; N, 5·7%).

2-o-, -m-, and -p-*Hydroxyphenylquinolines.*—*o*-Aminobenzaldehyde (1 g.) in ethanol (20 ml.) was added to the hydroxyacetophenone (1 g.) in ethanol (10 ml.), followed by 10% ethanolic sodium ethoxide (10 ml.). The mixture was warmed slightly and left at room temperature overnight. After removal of the solvent the solid residue was added to sufficient dilute hydrochloric acid to acidify the suspension, which was then extracted with ether to remove unchanged material. Subsequent neutralisation of the aqueous solution with sodium hydrogen carbonate precipitated the required compound. Thus were obtained: 2-o-*Hydroxyphenylquinoline*, yellow needles (from ethanol) (1·2 g.), m. p. 115—117° (Found: C, 81·3; H, 4·85; N, 6·65. $C_{15}H_{11}ON$ requires C, 81·5; H, 5·0; N, 6·3%) [*methiodide*, formed only in boiling methanol (4 hr.), yellow needles, m. p. 180° (decomp.) (Found: I, 34·7. $C_{16}H_{14}ONI$ requires I, 35·0%)].

2-m-*Hydroxyphenylquinoline*, colourless needles (from aqueous ethanol) (1 g.), m. p. 156—157° (Found: C, 81·3; H, 4·8; N, 6·4%) [*methiodide*, yellow needles, m. p. 194—195° (Found: I, 34·9%)].

2-p-*Hydroxyphenylquinoline*, colourless needles (from ligroin–benzene) (1·4 g.), m. p. 237—238° (Found: C, 81·5; H, 5·05; N, 6·5%) [*methiodide*, yellow needles, m. p. 209° (Found: I, 34·8%)], giving *betaine*, orange needles (from chloroform–benzene), m. p. 85·5° (Found: N, 5·6. $C_{16}H_{13}ON$ requires N, 5·96%).

3-Hydroxy-1-*methylpyridinium Iodide.*—This was obtained by boiling 3-hydroxypyridine in acetone under reflux with methyl iodide for 1 hr., as colourless prisms, m. p. 120·5° (Found: C, 28·2; H, 3·9; N, 5·5; I, 49·8. Calc. for C_6H_8ONI,H_2O: C, 28·4; H, 4·0; N, 5·5; I, 49·5%).

3-Hydroxy-1-p-*nitrobenzylpyridinium Bromide.*—A colourless solid was formed on boiling 3-hydroxypyridine in acetone with *p*-nitrobenzyl bromide for 1 hr., and recrystallised from ethanol (m. p. 216—217°) (Found: N, 8·15; Br, 23·8. Calc. for $C_{12}H_{11}O_3N_2Br$: N, 8·5; Br, 24·3%) [picrate, m. p. 177° (Found: N, 15·8. Calc. for $C_{18}H_{13}O_{10}N_5$: N, 15·3%); *betaine*, colourless (from chloroform–benzene), m. p. 177° (Found: C, 56·1; H, 4·0; N, 11·4. $C_{12}H_{10}O_3N_2,H_2O$ requires C, 56·7; H, 4·7; N, 11·3%).

[9] Chiang and Hartung, *J. Org. Chem.*, 1945, **10**, 21.

Spectra.—A Unicam quartz spectrophotometer SP.500 was used in the determination of the visible absorption spectra. The values for the absorption maxima of 8-hydroxy-1-methylquinolinium anhydro-salt (Table 1) were obtained for solutions prepared by diluting 1 ml. of a 0·00646M-solution in chloroform (washed with water and dried over potassium carbonate) to 25 ml. with the appropriate solvent. The infrared spectra were determined by using a Hilger spectrophotometer H 800 with a lithium fluoride prism. The phenol and *p*-nitrophenol were of " AnalaR " quality, and the ethanol was distilled off sodium.

The authors thank Dr. D. M. W. Anderson for determination of the infrared spectra and for helpful discussion.

THE UNIVERSITY, EDINBURGH, 9. [*Received, September 8th*, 1958.]

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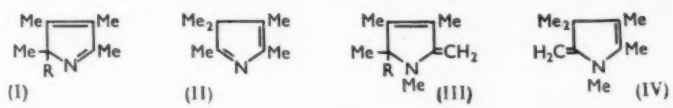
305. *The Alkylation of Tri- and Tetra-alkylpyrroles.*

By H. BOOTH, A. W. JOHNSON, E. MARKHAM, and R. PRICE.

The action of alkyl iodides on the Grignard derivatives of 2 : 3 : 4- and 2 : 3 : 5-trialkylpyrroles and 2 : 3 : 4 : 5-tetra-alkylpyrroles is shown to give tetra- and penta-alkyl-2*H*-pyrroles (pyrrolenines) containing 2 : 2-*gem*-dialkyl groups. The reaction is inhibited by the presence of ester substituents on the pyrrole ring.

ALTHOUGH the structure of the alkylation products of pyrroles caused a lengthy polemic some forty years ago, the subject has scarcely received comment since. In spite of all the early work it is impossible, because of the conflicting claims, to predict the position of alkylation in pyrrole rings containing varying numbers of alkyl groups. Ciamician and Anderlini [1] suggested 1 : 2-dihydropyridine structures for the base $C_9H_{15}N$ obtained by treating sodium pyrrole-2-carboxylate with methyl iodide in methanol and for the base $C_{10}H_{17}N$ from 1-methylpyrrole and methyl iodide in methanol in presence of potassium carbonate. Influenced by Plancher's work on the alkylation of indoles, Ciamician [2] later suggested that the pyrrole alkylation products were more likely to be derivatives of 2*H*-pyrrole (pyrrolenine) and this was eventually substantiated by Plancher himself,[3]



(I) (II) (III) (IV)

although the dihydropyridine structures were still favoured by some authors [4] as late as 1914. The base $C_9H_{15}N$ thus was recognised as a pentamethyl-2*H*-pyrrole or -3*H*-pyrrole although the precise location of the substituents was not established by Ciamician or Plancher, and Beilstein [5] gives the alternative structures, (I; R = Me) and (II), for the methylation product. However, in a related series, an unequivocal proof of structure was apparently obtained by Hess, Wissing, and Suchier [6] who claimed that methylation of 3-ethyl-2 : 5-dimethylpyrrole gave the same product as was formed by ethylation of 2 : 3 : 5-trimethylpyrrole, thus suggesting that in a 2 : 3 : 5-trialkylpyrrole, further alkylation occurs at the 3-(*i.e.* β-)position. It will be shown subsequently that the German experimental work was at fault and the conclusion incorrect.

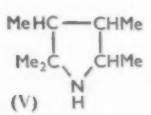
We have prepared the base $C_9H_{15}N$ from methyl iodide and the Grignard derivatives

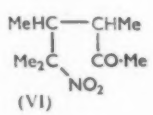
[1] Ciamician and Anderlini, *Gazzetta*, 1888, **18**, 557; 1889, **19**, 102; *Ber.*, 1888, **21**, 2855; 1889, **22**, 656; Anderlini, *Gazzetta*, 1890, **20**, 61; *Ber.*, 1889, **22**, 2506.
[2] Ciamician, *ibid.*, 1904, **37**, 4200.
[3] Plancher *et al.*, *Atti R. Accad. Lincei*, 1913, **22**, ii, 599, 703, 708; 1914, **23**, ii, 412.
[4] Oddo and Mameli, *Gazzetta*, 1913, **43**, 504; Hess and Wissing, *Ber.*, 1914, **47**, 1416.
[5] *Beilstein's Handbuch*, 1935, **20**, 180.
[6] Hess, Wissing, and Suchier, *Ber.*, 1915, **48**, 1865.

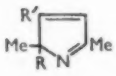
of either 2 : 5-dimethylpyrrole or 2 : 3 : 4 : 5-tetramethylpyrrole [7] and its structure is shown to be 2 : 2 : 3 : 4 : 5-pentamethyl-2*H*-pyrrole (I; R = Me). Thus, ozonolysis of the base gave diacetyl in 23% yield but no 3 : 3-dimethylpentane-2 : 4-dione which would have been formed from structure (II). The nitrogen was obtained from the ozonolysis product as ammonia. Further evidence for structure (I; R = Me) was obtained by treating the corresponding methiodide with alkali; the anhydro-base, identical with Ciamician's base $C_{10}H_{17}N$ referred to above, was then obtained. The ultraviolet spectrum of this compound (max. at 212 and 287 mμ) indicated the presence of a conjugated system as in (III; R = Me) whereas the corresponding structure (IV) derived from (II) would not contain this feature.

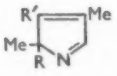
Reduction of the 2*H*-pyrrole (I; R = Me) with sodium and alcohol gave 2 : 2 : 3 : 4 : 5-pentamethylpyrrolidine (V), characterised as the picrolonate, m. p. 227—230°, and attempts were made to synthesise this and the isomeric-2 : 3 : 3 : 4 : 5-pentamethylpyrrolidine for comparison. Addition of 2-nitropropane to 3-methylpent-3-en-2-one in the presence of diethylamine [8] gave the γ-nitro-ketone (VI), probably as a mixture of two racemates, which was reductively cyclised in the presence of Raney nickel. Two picrolonates, m. p. 196—198° and 242—244° respectively, neither of which corresponded to that obtained from reduction of the 2*H*-pyrrole, were isolated from the hydrogenation product. γ-Nitro-ketones are said [8] to yield predominantly one form of the pyrrolidine when the hydrogenation is carried out in presence of ammonia, and in the case of the ketone (VI) the pyrrolidine formed in this manner yielded the picrolonate, m. p. 196—198°, identical with that already obtained. As the pyrrolidine (V) can exist in four racemic forms and as attempts to obtain 2 : 3 : 3 : 4 : 5-pentamethylpyrrolidine by addition of nitroethane to 3 : 4-dimethylpent-3-en-2-one and subsequent reduction were uniformly unsuccessful, this approach was abandoned.

The formulation (I; R = Me) of the methylation product of 2 : 3 : 4 : 5-tetramethylpyrrole was confirmed by the discovery that the picrate of 2-ethyl-2 : 3 : 4 : 5-tetramethyl-2*H*-pyrrole (I; R = Et) formed by ethylation of 2 : 3 : 4 : 5-tetramethylpyrrole was identical with that derived from a base obtained by the methylation of 2-ethyl-3 : 4 : 5-trimethylpyrrole.[7] A second base, presumably 5-ethyl-2 : 2 : 3 : 4-tetramethyl-2*H*-pyrrole, was also formed in this alkylation but it was not isolated pure. Each of the alkylation products (I; R = Et) was converted through the methiodide into the anhydro-base (III; R = Et) and once again identical picrates were isolated. The ultraviolet spectra of (III; R = Et) and (III; R = Me) were also identical.


(V)


(VI)


(VII)


(VIII)

Once the structure of the 2*H*-pyrrole (I; R = Me) had been established it became of interest to consider the claim [6] that further alkylation of 2 : 3 : 5-trialkylpyrroles occurred at the 3-position, and we have therefore repeated the German work. Two products are obtained in each of these alkylations, a 2 : 2 : 3 : 5-tetra-alkyl-2*H*-pyrrole (VII) and a 2 : 2 : 3 : 4 : 5-penta-alkyl-2*H*-pyrrole (I). Thus the methylation of 3-ethyl-2 : 5-dimethylpyrrole [7] gives a mixture of 3-ethyl-2 : 2 : 5-trimethyl-2*H*-pyrrole (VII; R = Me, R′ = Et) and 3-ethyl-2 : 2 : 4 : 5-tetramethyl-2*H*-pyrrole whereas the ethylation of 2 : 3 : 5-trimethylpyrrole [7] gives a mixture of 2-ethyl-2 : 3 : 5-trimethyl-2*H*-pyrrole (VII; R = Et, R′ = Me) and 2 : 4-diethyl-2 : 3 : 5-trimethyl- or 2 : 3-diethyl-2 : 4 : 5-trimethyl-2*H*-pyrrole. It was the two bases (VII; R = Me, R′ = Et and R = Et, R′ = Me) which the German authors claimed to be identical on the basis of the apparent identity (mixed m. p.) of the

[7] Johnson, Markham, Price, and Shaw, *J.*, 1958, 4254.
[8] Kloetzel, *J. Amer. Chem. Soc.*, 1947, **69**, 2271.

respective picrates. It is true that these derivatives melt with decomposition at approximately the same temperature and that there is little depression of this decomposition point when they are mixed, but the crystalline form and the solubilities of the picrates differ markedly and the melting points of the picrolonates differ by about 40°. In addition the picrate of one of the corresponding anhydro-bases (from VII; R = Et, R′ = Me) is crystalline but the other was obtained only as an oil. The structure (VII; R = Et, R′ = Me) was confirmed by its identity (picrate, picrolonate, and picrate of the corresponding anhydro-base) with the tetra-alkyl-2*H*-pyrrole obtained by methylation of 5-ethyl-2 : 4-dimethylpyrrole.[7] The penta-alkyl-2*H*-pyrrole also formed in the last reaction was 2-ethyl-2 : 3 : 4 : 5-tetramethyl-2*H*-pyrrole (I; R = Et) identical with the product of ethylation of 2 : 3 : 4 : 5-tetramethylpyrrole or of methylation of 2-ethyl-3 : 4 : 5-trimethylpyrrole described above.

Thus in the alkylation of 2 : 3 : 5-trialkylpyrroles by the Grignard reaction, the main reaction is α-substitution at the 2-(but not 5-)position of the pyrrole to give a 2 : 2 : 3 : 5-tetra-alkyl-2*H*-pyrrole (max. at *ca.* 237 mμ in neutral and 255 mμ in acid solution); the subsidiary reaction is β-substitution at the 4-position to give the tetra-alkylpyrrole which is then alkylated to the 2 : 2 : 3 : 4 : 5-penta-alkyl-2*H*-pyrrole (max. at *ca.* 242 mμ in neutral and 269 mμ in acid solution).

The alkylation of 2 : 3 : 4-trialkylpyrroles is of interest because of its connection with the biogenesis of porphyrins[9] and it is now shown that the products are 2 : 3 : 4 : 5-tetra-alkylpyrroles and 2 : 2 : 3 : 4-tetra-alkyl-2*H*-pyrroles (VIII) (max. at *ca.* 248 mμ in neutral and 271 mμ in acid solution). Alkylation at the α-position is postulated in this series partly because of the non-identity of the 2 : 2 : 3 : 4-tetra-alkyl-2*H*-pyrroles (VIII; R = Me, R′ = Et and R = Et, R′ = Me respectively) obtained from the methylation of cryptopyrrole and the ethylation of 2 : 3 : 4-trimethylpyrrole, and partly by analogy with the earlier series. The ratio of tetra-alkylpyrroles to tetra-alkyl-2*H*-pyrroles in the alkylation products of the 2 : 3 : 4-trialkylpyrroles varied appreciably according to the nature of the substituent. Thus phyllopyrrole was a minor product from the methylation of cryptopyrrole whereas only the tetra-substituted pyrrole was isolated from the methylation of 3-ethoxycarbonylmethyl-2 : 4-dimethylpyrrole, and 5-ethyl-2 : 3 : 4-trimethylpyrrole was the major product of ethylation of 2 : 3 : 4-trimethylpyrrole.

A complex mixture has been obtained from the methylation of 2 : 5-dimethylpyrrole. Besides 2 : 2 : 3 : 4 : 5-pentamethyl-2*H*-pyrrole already mentioned, 2 : 3 : 4 : 5-tetramethylpyrrole and two isomeric tetramethyl-2*H*-pyrroles, probably 2 : 2 : 3 : 5- and 2 : 2 : 4 : 5-substituted, were obtained. Although alkylation of alkylpyrroles is thus a relatively easy reaction, it is inhibited by electron-attracting substituents attached directly to the ring. Thus the Grignard derivative of 3-ethoxycarbonyl-2 : 4-dimethylpyrrole was not methylated further under the conditions used throughout the present work. Under these conditions, *i.e.* methylation of the Grignard derivative of the pyrrole with methyl iodide, no evidence for substitution at the β-position of the pyrrole ring has been obtained. Other methods of methylation are under examination. If the mode of methylation in Nature is also electrophilic then the methylation step in the biogenesis of vitamin B_{12} from porphobilinogen is unlikely to involve a porphyrinogen.

Experimental

Ultraviolet absorption spectra were determined in 95% ethanol except where otherwise stated.

2 : 2 : 3 : 4 : 5-*Pentamethyl*-2H-*pyrrole* (I; R = Me).—(*a*) 2 : 5-Dimethylpyrrole[10] (62 g.) in dry ether (300 c.c.) was added to a solution of methylmagnesium iodide [from magnesium (15·8 g.) and methyl iodide (93 g.)] in dry ether (300 c.c.), and the mixture was heated under reflux for 1 hr. More methyl iodide (93 g.) was added, and the mixture heated under reflux for

[9] Bullock, Johnson, Markham, and Shaw, *J.*, 1958, 1430.
[10] Young and Allen, *Org. Syntheses*, Coll. Vol. II, 1943, p. 219.

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a further 18 hr. The solution was cooled (ice) and treated with saturated ammonium chloride solution (200 c.c.), and the ethereal layer separated. The aqueous solution was washed with ether and the combined ethereal solutions were thoroughly extracted with N-hydrochloric acid. The acid extracts were neutralised with sodium hydroxide solution and again extracted with ether. After removal of solvent from the dried extract, the residual oil was distilled and the following fractions were collected: (i) oil (4·0 g.), b. p. up to 64°/14 mm.; (ii) pale yellow oil (2·4 g.), b. p. 64—80°/14 mm.; (iii) pale yellow oil (2·4 g.), b. p. 80—86°/14 mm.; and (iv) solid (3·0 g.), b. p. 86—88°/14 mm. Fraction (i), consisting largely of tetramethyl-2*H*-pyrroles, was redistilled and three main fractions were collected: (*ia*) oil (1·1 g.), b. p. 30—36°/14 mm.; (*ib*) oil (0·7 g.), b. p. 36—45°/14 mm.; and (*ic*) oil (0·9 g.), b. p. 45—52°/14 mm. Fraction (*ia*) showed $\lambda_{max.}$ 233 mμ, log ε 3·38, and in dilute ethanolic hydrochloric acid, $\lambda_{max.}$ 250 mμ, log ε 3·47. [*Picrate*, yellow needles (ethanol), m. p. 169—170° (Found: C, 48·0; H, 4·85; N, 16·2. $C_{14}H_{16}O_7N_4$ requires C, 47·7; H, 4·6; N, 15·9%). *Picrolonate*, yellow needles (ethanol), m. p. 197—198° (Found: C, 55·9; H, 5·4; N, 18·5. $C_{18}H_{21}O_5N_5$ requires C, 55·8; H, 5·45; N, 18·1%).] Fraction (*ib*) showed $\lambda_{max.}$ 236 mμ, log ε 3·42, and in dilute ethanolic hydrochloric acid, $\lambda_{max.}$ 255 mμ, log ε 3·48. [*Picrate*, yellow plates (ethanol), m. p. 195—196° (Found: C, 47·9; H, 4·65; N, 15·7. $C_{14}H_{16}O_7N_4$ requires C, 47·7; H, 4·6; N, 15·9%). *Picrolonate*, yellow plates (ethanol), m. p. 202—203° (Found: C, 55·8; H, 5·6; N, 17·8. $C_{18}H_{21}O_5N_5$ requires C, 55·8; H, 5·45; N, 18·1%).] Fraction (*ic*) yielded the same derivatives as those obtained from fraction (*ib*).

Fraction (ii), consisting largely of 2 : 2 : 3 : 4 : 5-pentamethyl-2*H*-pyrrole, was converted into the picrate, which formed yellow plates (ethanol), m. p. 167—168° (lit.,[11] 168—169°) (Found: C, 49·0; H, 5·0; N, 15·7. Calc. for $C_{15}H_{18}O_7N_4$: C, 49·2; H, 5·0; N, 15·3%). A sample of the base regenerated (lithium hydroxide) from the picrate had b. p. 51—53°/12 mm., n_D^{25} 1·4573; (i) $\lambda_{max.}$ 243 mμ, log ε 3·40, (ii) in dilute ethanolic hydrochloric acid, $\lambda_{max.}$ 266 mμ, log ε 3·45. [*Picrolonate*, yellow plates (ethanol), m. p. 219—221° (Found: C, 56·5; H, 5·8. $C_{19}H_{23}O_5N_5$ requires C, 56·85; H, 5·8%). *Methiodide*, prisms (acetone–ethyl acetate), m. p. 173—174° (Found: C, 42·9; H, 6·5. $C_{10}H_{18}NI$ requires C, 43·0; H, 6·5%); $\lambda_{max.}$ in ethanol at 218 (iodide) and 270 mμ (log ε 4·18 and 3·75). Methopicrate, orange needles (water), m. p. 144—146° (lit.,[11] 148°) (Found: C, 50·3; H, 5·1; N, 14·7. Calc. for $C_{16}H_{20}O_7N_4$: C, 50·5; H, 5·3; N, 14·7%).] Treatment of the methiodide with aqueous sodium hydroxide followed by ether extraction gave 1 : 3 : 4 : 5 : 5-pentamethyl-2-methylene-Δ^3-pyrroline, b. p. 126—128° (bath temp.)/68 mm., n_D^{19} 1·5070, $\lambda_{max.}$ 212 and 287 mμ (log ε 4·06 and 3·83 respectively) (in hexane). The derived picrate crystallised from water in orange needles, m. p. 144—145° undepressed when mixed with the methopicrate of 2 : 2 : 3 : 4 : 5-pentamethyl-2*H*-pyrrole.

Fraction (iv) of the original distillation was a solid which crystallised from light petroleum as plates, m. p. 110° (lit.,[7] 110°). The picrate formed yellow-brown prisms (ethanol), m. p. 127° not depressed on admixture with an authentic specimen of 2 : 3 : 4 : 5-tetramethylpyrrole picrate.

(*b*) 2 : 3 : 4 : 5-Tetramethylpyrrole [7] (8 g.) in ether (30 c.c.) was added slowly to a solution of methylmagnesium iodide, prepared from magnesium (1·44 g.) and methyl iodide (8·45 g.) in dry ether (20 c.c.), and the mixture kept overnight. Methyl iodide (8·45 g.) was added next day, and the solution heated under reflux for 20 hr. and then cooled to 0°. A saturated solution of ammonium chloride (50 c.c.) was added and the ethereal layer separated. The aqueous solution was extracted several times with ether and the combined ethereal extracts were shaken repeatedly with N-hydrochloric acid. The acid extracts were made alkaline with sodium hydroxide solution and again extracted with ether. After removal of the solvent from the dried extract, the residue was distilled, and 2 : 2 : 3 : 4 : 5-pentamethyl-2*H*-pyrrole collected, b. p. 80°/40 mm. (3·15 g.; 35·5%). The picrate, m. p. 167—168°, was identical with that obtained in the previous experiment.

2 : 2 : 3 : 4 : 5-*Pentamethylpyrrolidine* (V).—(*a*) Sodium (3·3 g.) was added gradually to a solution of 2 : 2 : 3 : 4 : 5-pentamethyl-2*H*-pyrrole (0·82 g.) in dry ethanol (25 c.c.). The mixture was heated under reflux for 1 hr., cooled, diluted with aqueous ethanol (75%; 20 c.c.) and then acidified with hydrochloric acid. The alcohol was removed by distillation, and the residue dissolved in water (20 c.c.) and made alkaline with aqueous sodium hydroxide. The solution was then extracted several times with ether, the ethereal extracts were dried, and the solvent was removed. Distillation of the residue gave an oil (0·5 g.; 60%), b. p. 122—124° (bath

[11] Plancher and Zambonini, *Atti R. Accad. Lincei*, 1913, **22**, ii, 708.

temp.)/200 mm. The *picrolonate* formed yellow prisms (acetone), m. p. 227—230° (decomp.) (Found: C, 56·6; H, 6·7; N, 17·7. $C_{19}H_{27}O_5N_5$ requires C, 56·3; H, 6·7; N, 17·3%).

(*b*) Raney nickel (4·0 g.; washed with methanol) was added to a solution of 3 : 4 : 5-trimethyl-5-nitrohexan-2-one (8·0 g.; see below) in methanol (50 c.c.), and the mixture hydrogenated at 50 atm. and 105° for 90 min. After removal of the catalyst, the solution was acidified with hydrochloric acid, and the methanol removed by distillation. The solution of the residue in water (20 c.c.) was made alkaline (aqueous sodium hydroxide) and repeatedly extracted with ether. After removal of the solvent from the dried ethereal extract and distillation the product was obtained as an oil (1·2 g.; 20%), b. p. (bath temp.) 125—130°/190 mm. The product gave two picrolonates which were separated by fractional crystallisation from acetone: (i) m. p. 196—198° (decomp.), yellow cubes (Found: C, 56·0; H, 6·4; N, 16·9%); (ii) m. p. 242—244° (decomp.), yellow cubes, but the amount obtained was not sufficient for analysis.

(*c*) The nitro-hexanone (2·0 g.) was dissolved in a mixture of methanol (30 c.c.) and aqueous ammonia (1 c.c.; *d* 0·88). Raney nickel (1 g.; washed with methanol) was added, and the mixture hydrogenated at 50 atm. at 100° for 90 min. The product (0·17 g., 11·5%), b. p. 115—120°/156 mm., was isolated as in the foregoing experiment. The picrolonate which formed yellow cubes (acetone) had m. p. 195—197°, not depressed on admixture with that obtained above.

3 : 4 : 5-*Trimethyl*-5-*nitrohexan*-2-*one* (VI).—3-Methylpent-3-en-2-one (46·7 g.), 2-nitropropane (425 g.), and diethylamine (34·8 g.) were heated under reflux for 20 hr. The unchanged reagents were removed by distillation (up to 55°/20 mm.), and the residue was distilled, the fraction boiling at 125—128°/10—12 mm. being collected as a pale yellow oil (19·1 g.; 21%). The *semicarbazone* formed prisms (ethanol), m. p. 186—187° (Found: N, 23·0. $C_{10}H_{20}O_3N_4$ requires N, 22·95%).

Ozonolysis of 2 : 2 : 3 : 4 : 5-*Pentamethyl*-2H-*pyrrole*.—A solution of the pentamethyl-2*H*-pyrrole (1·0 g.) in dry chloroform (15 c.c.) was cooled (ice), and a slow stream of ozonised oxygen passed through it for 5 hr. Acetic acid (10 c.c.) and zinc dust (1·0 g.) were added and the mixture was heated under reflux for 15 min. The excess of zinc was removed, and the filtrate distilled in steam, the first fraction (50 c.c.) of the distillate being collected (distillate *A*). The residue in the distillation flask was made alkaline with sodium hydroxide and again distilled in steam, the first fraction (20 c.c.) again being collected (distillate *B*). Phenylhydrazine (0·5 g.) was added to distillate *A*, and the mixture heated on the steam-bath for 30 min. The yellow precipitate, which was obtained when the solution was cooled, was separated, washed with a little ethanol, and crystallised from nitrobenzene; it formed fawn-coloured crystals (0·25 g; 23·5%), m. p. 239—242° not depressed when mixed with an authentic specimen of diacetyl osazone (Found: N, 21·5. Calc. for $C_{16}H_{18}N_4$: N, 21·05%). Addition of picric acid (0·5 g.) to distillate *B* gave ammonium picrate (0·36 g., 20·1%) which formed yellow needles, m. p. (sealed tube) 270—272° (decomp.) (Found: N, 22·4. Calc. for $C_6H_6O_7N_4$: N, 22·75%).

2-*Ethyl*-2 : 3 : 4 : 5-*tetramethyl*-2H-*pyrrole* (I; R = Et).—(*a*) The Grignard derivative of 2 : 3 : 4 : 5-tetramethylpyrrole (10·2 g.) was ethylated with ethyl iodide (17 g.) in the manner already described for methylation. The product was treated similarly and distilled under reduced pressure to give the base as a pale yellow oil (5·9 g., 47%), b. p. 98—100°/72 mm. The *picrate* formed golden yellow needles (ethanol), m. p. 177—178° (Found: C, 50·6; H, 5·5; N, 14·9. $C_{16}H_{20}O_7N_4$ requires C, 50·5; H, 5·3; N, 14·7%). Light absorption of the base regenerated from the picrate: (i) $\lambda_{max.}$ 241 mμ, log ε 3·50, (ii) in ethanolic hydrochloric acid $\lambda_{max.}$ 268 mμ, log ε 3·62.

(*b*) The Grignard derivative of 2-ethyl-3 : 4 : 5-trimethylpyrrole [7] (4·4 g.) was methylated in the usual manner. The product, a mixture of 2-ethyl-2 : 3 : 4 : 5-tetramethyl- and (presumably) 5-ethyl-2 : 2 : 3 : 4-tetramethyl-2*H*-pyrrole, formed a pale yellow oil (1·6 g., 33%), b. p. 106—112°/78 mm. The picrate formed yellow needles, m. p. 176—177° after repeated crystallisation from ethanol. The m. p. of a mixture with the product from the previous experiment was 176—177° (Found: C, 50·6; H, 5·4; N, 14·8%).

(*c*) 2-Ethyl-3 : 5-dimethylpyrrole [7] (18·7 g.) was methylated with methyl iodide in the usual manner. The basic oil so obtained was fractionated and three main fractions were collected: (i) oil (2·05 g.), b. p. 58—66°/13 mm.; (ii) oil (1·8 g.), b. p. 68—78°/13 mm.; and (iii) pale yellow oil (2·2 g.), b. p. 80—88°/13 mm. Fractions (i) and (ii) gave identical picrates and were combined and treated separately (see below; 2-ethyl-2 : 3 : 5-trimethyl-2*H*-pyrrole). Fraction

(iii) was converted into the picrate which formed yellow needles (ethanol), m. p. 174—176°, not depressed on admixture with the picrates from the previous two experiments (Found: C, 50·2; H, 5·5; N, 14·8%).

5-Ethyl-1 : 3 : 4 : *5-tetramethyl*-2-*methylene*-Δ^3-*pyrroline* (III; R = Et).—(i) 2-Ethyl-2 : 3 : 4 : 5-tetramethyl-2*H*-pyrrole from the ethylation of 2 : 3 : 4 : 5-tetramethylpyrrole (above) was converted into its methiodide, m. p. 162—163°. The methiodide (2·0 g.) was added to a solution of potassium hydroxide (1·5 g.) in water (10 c.c.), and the resulting oil extracted with ether (3 × 10 c.c.). The solvent was removed from the dried ether extract, and the residue distilled to give a pale yellow oil (0·7 g., 62%), b. p. (bath temp.) 115—120°/35 mm., $\lambda_{max.}$ (ethanol), 209 and 272 mμ, log ε 3·80 and 3·62, respectively. The *picrate* formed yellow prisms (ethanol), m. p. 134—135° (Found: C, 52·1; H, 5·6; N, 14·3. $C_{17}H_{22}O_7N_4$ requires C, 51·8; H, 5·6; N, 14·2%).

(ii) The mixed bases obtained from the methylation of 2-ethyl-3 : 4 : 5-trimethylpyrrole (above) were converted into the methiodides, which had m. p. 138—146° and were treated directly (1·7 g.) with alkali as above to give the mixed anhydro-bases (0·5 g.), b. p. (bath temp.) 115—124°/35 mm.; $\lambda_{max.}$ 210 and 270 mμ, log ε 3·68 and 3·70. The corresponding picrate formed yellow prisms (ethanol), m. p. 133—134° after repeated crystallisation, not depressed on admixture with the picrate obtained in the previous experiment (Found: C, 51·5; H, 5·4; N, 14·6%).

2-Ethyl-2 : 3 : *5-trimethyl*-2H-*pyrrole* (VII; R = Et, R′ = Me).—(i) Fractions (i) and (ii) from the methylation product of 2-ethyl-3 : 5-dimethylpyrrole (above) were combined (3·85 g.) and redistilled, the main fraction (2·4 g.), b. p. 52—56°/11 mm., being obtained as an oil with strong camphoraceous odour; $\lambda_{max.}$ (ethanol) 237 mμ, log ε 3·50, $\lambda_{max.}$ (ethanolic hydrochloric acid) 255 mμ, log ε 3·54. The *picrate* formed yellow plates (ethanol), m. p. 193—195° after sintering and darkening about 175° (Found: C, 49·2; H, 5·1; N, 15·4. $C_{15}H_{18}O_7N_4$ requires C, 49·2; H, 4·95; N, 15·3%). The *picrolonate* formed yellow needles (ethanol), m. p. 165—166° (Found: C, 56·9; H, 5·9; N, 17·4. $C_{19}H_{23}O_5N_5$ requires C, 56·85; H, 5·8; N, 17·45%).

(ii) 2 : 3 : 5-Trimethylpyrrole [7] (47·2 g.) was ethylated with ethyl iodide. The basic oil so obtained was distilled and the following fractions were collected: (i) oil (7·8 g.), b. p. 58—68°/18 mm.; (ii) oil (12·7 g.), b. p. 76—90°/18 mm.; (iii) pale yellow oil (3·9 g.), b. p. 92—98°/18 mm., which was treated separately (see below; 2 : 4-diethyl-2 : 3 : 5-trimethyl-2*H*-pyrrole). Fractions (i) and (ii), which gave identical picrates, were combined and re-distilled, the fraction, b. p. 54—56°/12 mm., being collected as an oil (6·1 g.) with camphoraceous odour; $\lambda_{max.}$ (in ethanol) 235 mμ, log ε 3·49, $\lambda_{max.}$ (in ethanolic hydrochloric acid) 254 mμ, log ε 3·60. Picrate, yellow plates (ethanol), m. p. 194—195° (with previous darkening) not depressed on admixture with the picrate of the base prepared in the foregoing experiment (Found: C, 49·2; H, 4·95; N, 15·0%). Picrolonate, golden-yellow needles (ethanol), m. p. 166—167° again undepressed by admixture with the foregoing picrolonate (Found: C, 56·6; H, 5·9; N, 17·1%).

5-Ethyl-1 : 4 : *5-trimethyl*-2-*methylene*-Δ^3-*pyrroline*.—(i) 2-Ethyl-2 : 3 : 5-trimethyl-2*H*-pyrrole, obtained from the ethylation of 2 : 3 : 5-trimethylpyrrole (above), was converted into the methiodide, m. p. 204—208°, which (1·9 g.) was converted into the anhydro-base by the action of alkali. The base (0·65 g.; 63%) was obtained as a pale yellow oil, b. p. (bath temp.) 110—115°/50 mm.; $\lambda_{max.}$ 210 mμ (log ε 3·94), 288 mμ (log ε 3·66). The *picrate* formed small yellow needles (ethanol), m. p. 160—164° (with previous darkening) (Found: C, 50·4; H, 5·65; N, 14·7. $C_{16}H_{20}O_7N_4$ requires C, 50·5; H, 5·3; N, 14·7%).

(ii) The same 2*H*-pyrrole, obtained from the methylation of 3 : 5-dimethyl-2-ethylpyrrole (above), was similarly converted through the methiodide into the anhydro-base; $\lambda_{max.}$ 211 mμ (log ε 3·94), 290 mμ (log ε 3·63). The corresponding picrate (Found: C, 50·2; H, 5·35; N, 14·8%) had m. p. 160—162°, not depressed on admixture with the picrate obtained from the previous experiment.

2 : 4-*Diethyl*-2 : 3 : *5-trimethyl*- *or* 2 : 3-*Diethyl*-2 : 4 : *5-trimethyl*-2H-*pyrrole*.—The high-boiling fraction from the ethylation of 2 : 3 : 5-trimethylpyrrole was converted into the *picrate*, which formed yellow needles (ethanol), m. p. 140—141° (Found: C, 51·8; H, 5·45; N, 14·2. $C_{17}H_{22}O_7N_4$ requires C, 51·8; H, 5·6; N, 14·2%). The free base (0·6 g.), b. p. (bath temp.) 95—100°/32 mm., was regenerated from the picrate by aqueous lithium hydroxide. It had light absorption: (i) in ethanol, $\lambda_{max.}$ 242 mμ, log ε 3·55; (ii) in ethanolic hydrochloric acid, $\lambda_{max.}$ 267 mμ, log ε 3·66. *Picrolonate*, yellowish-brown needles (ethanol), m. p. 144—146° (Found: C, 58·9; H, 6·25; N, 15·9. $C_{21}H_{27}O_5N_5$ requires C, 58·75; H, 6·35; N, 16·3%).

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3-Ethyl-2 : 2 : 5-trimethyl-2H-pyrrole (VII; R = Me, R′ = Et).—3-Ethyl-2 : 5-dimethylpyrrole [7] was methylated with methyl iodide. The basic oil so obtained was distilled and the following fractions were collected: (i) oil (3·4 g.), b. p. 68—78°/11 mm.; (ii) pale yellow oil (5·1 g.), b. p. 82—88°/11 mm.; (iii) pale yellow oil (3·5 g.), b. p. 88—92°/11 mm. Fraction (i) was redistilled, and the fraction (2·6 g.), 70—72°/11 mm., collected. This oil, of the usual camphoraceous odour, had light absorption: (i) in ethanol, $\lambda_{max.}$ 235 mμ, log ε 3·48; (ii) in ethanolic hydrochloric acid, $\lambda_{max.}$ 257 mμ, log ε 3·56. The *picrate* (Found: C, 49·2; H, 4·75; N, 15·4. $C_{15}H_{18}O_7N_4$ requires C, 49·2; H, 4·95; N, 15·3%) formed yellow needles (ethanol), m. p. 189—190°, mixed m. p. 190—192° (darkening *ca.* 170°) with the picrate (m. p. 194—195°) of 2-ethyl-2 : 3 : 5-trimethyl-2*H*-pyrrole (above). The *picrolonate* formed pale yellow prisms (ethanol), m. p. 200—203° (Found: C, 57·1; H, 5·5; N, 17·8. $C_{19}H_{23}O_5N_5$ requires C, 56·85; H, 5·8; N, 17·45%).

4-Ethyl-1 : 5 : 5-trimethyl-2-methylene-Δ³-pyrroline.—The methiodide (1·6 g.), m. p. 195—197°, of 3-ethyl-2 : 2 : 5-trimethyl-2*H*-pyrrole was converted into the anhydro-base by the action of alkali. The pale yellow product (0·5 g.; 57%) had b. p. (bath temp.) 110—115°/45 mm.; $\lambda_{max.}$ (ethanol) 210 and 290 mμ, log ε 3·85 and 3·58. Neither the picrate nor the picrolonate could be obtained solid.

4-Ethyl-2 : 2 : 3 : 5-tetramethyl- or 3-Ethyl-2 : 2 : 4 : 5-tetramethyl-2H-pyrrole.—Fraction (ii) from the methylation of 3-ethyl-2 : 5-dimethylpyrrole was converted into the *picrate*, yellow needles, m. p. 161—162° after crystallisation from ethanol (Found: C, 50·3; H, 5·3; N, 14·8. $C_{16}H_{20}O_7N_4$ requires C, 50·5; H, 5·3; N, 14·7%). The free base was regenerated from the picrate (3·2 g.) by the action of aqueous lithium hydroxide and distilled. It was a pale yellow oil (0·45 g.) with the usual camphor-like odour, b. p. (bath temp.) 85—90°/40 mm.; $\lambda_{max.}$ in ethanol 244 mμ, log ε 3·34, $\lambda_{max.}$ in ethanolic hydrochloric acid 269 mμ, log ε 3·42. The *picrolonate* formed yellow prisms (ethanol), m. p. 203° (Found: C, 57·8; H, 6·05; N, 16·8. $C_{20}H_{25}O_5N_5$ requires C, 57·8; H, 6·05; N, 16·85%).

2-Ethyl-2 : 3 : 4-trimethyl-2H-pyrrole (VIII; R = Et, R′ = Me).—2 : 3 : 4-Trimethylpyrrole [7] (33·4 g.) was converted into the Grignard derivative and ethylated with ethyl iodide. The product was treated with saturated ammonium chloride solution (100 c.c.), and the basic fraction separated by extraction into N-hydrochloric acid and then back again into ether after neutralisation of the acid extract. The solvent was removed, and the residue fractionated under reduced pressure, the following fractions being collected: (i) oil (3·3 g.), b. p. 70—88°/14 mm.; (ii) pale yellow oil (11·8 g.), b. p. 88—96°/14 mm.; (iii) pale yellow oil (6·7 g.), b. p. 96—98°/14 mm. Fraction (i) was redistilled, and the product collected of b. p. 74—78°/14 mm. (1·2 g.); $\lambda_{max.}$ 248 mμ, log ε 3·49, $\lambda_{max.}$ in dilute ethanolic hydrochloric acid 271 mμ, log ε 3·58. The *picrate* formed yellow needles (ethanol), m. p. 156—157° which was not depressed on admixture with the picrate of the base obtained by methylation of 3-ethyl-2 : 4-dimethylpyrrole although it is a different compound (Found: C, 49·3; H, 5·2; N, 15·2. $C_{15}H_{18}O_7N_4$ requires C, 49·2; H, 4·95; N, 15·3%). The *picrolonate* formed yellow prisms (ethanol), m. p. 166—168° depressed to 136—146° on admixture with the picrolonate of the base obtained by methylation of 3-ethyl-2 : 4-dimethylpyrrole (Found: C, 56·9; H, 6·0; N, 17·4. $C_{19}H_{23}O_5N_5$ requires C, 56·85; H, 5·8; N, 17·45%).

Fractions (ii) and (iii) were combined and redistilled to give 5-ethyl-2 : 3 : 4-trimethylpyrrole [7] (15·7 g.; 42·5%), b. p. 94—96°/15 mm. (Found: C, 78·6; H, 10·8. Calc. for $C_9H_{15}N$: C, 78·8; H, 11·0%).

3-Ethyl-2 : 2 : 4-trimethyl-2H-pyrrole (VIII; R = Me, R′ = Et).—Freshly distilled cryptopyrrole (25 g.) was converted into the Grignard derivative which was treated with methyl iodide. The product was decomposed by addition of saturated ammonium chloride solution, and the ethereal layer extracted with N-hydrochloric acid. The solvent was removed from the neutral fraction, and the residue distilled at 97—110°/15 mm. to give a pale yellow solid which was purified by sublimation at 80°/14 mm. Phyllopyrrole was then obtained as plates (2·3 g.), m. p. 68—69° (lit.[12] m. p. 67°) after crystallisation from light petroleum. The picrate formed yellow prisms (ethanol), m. p. 104—105° (lit.[13] m. p. 104—105°) (Found: N, 15·3. Calc. for $C_{15}H_{18}O_7N_4$: N, 15·3%).

The acidic extracts were neutralised with aqueous ammonia (*d* 0·88) and extracted with ether (3 × 20 c.c.). The combined ethereal extracts were dried, the solvent was removed, and the

[12] Fischer, Baumann, and Riedl, *Annalen*, 1929, **475**, 205.
[13] Fischer and Klarer, *ibid.*, 1926, **450**, 181.

XUM

residue fractionated. Fraction (i) had b. p. 75—95°/22 mm. (5·3 g.); $\lambda_{max.}$ 251 mμ, log ε 3·42, $\lambda_{max.}$ in dilute hydrochloric acid 273 mμ, log ε 3·47. Fraction (ii), b. p. 95—100°/22 mm. (1·0 g.). The *picrate*, m. p. 158—160°, from fraction (i) formed yellow needles (ethanol) (Found: C, 49·3; H, 5·0; N, 15·4. $C_{15}H_{18}O_7N_4$ requires C, 49·2; H, 4·95; N, 15·3%). The *picrolonate*, m. p. 170°, from fraction (i) formed yellow prisms (ethanol) (Found: C, 57·0; H, 5·8; N, 17·45. $C_{19}H_{23}O_5N_5$ requires C, 56·85; H, 5·8; N, 17·45%). Fraction (ii) appeared to be the 3-ethyl-2 : 2 : 4-trimethyl-2*H*-pyrrole of fraction (i) contaminated with phyllopyrrole.

3-*Ethoxycarbonylmethyl*-2 : 4 : 5-*trimethylpyrrole*.—The Grignard derivative of 3-ethoxycarbonylmethyl-2 : 4-dimethylpyrrole [7] (1·0 g.) was treated with methyl iodide (0·73 g.) in dry ether (10 c.c.), and the suspension heated under reflux for 1 hr. More methyl iodide (3·65 g.) was added, and the suspension heated for 4 hr., cooled to 0°, and decomposed by the addition of saturated ammonium chloride solution (30 c.c.). The ethereal layer was separated, the aqueous layer washed with ether, and the combined ethereal extracts were washed and dried, and the solvent was removed. The residual oil was distilled, and the fraction, b. p. 165—168° (bath temp.)/10 mm. (0·05 g.; 5%), collected as an oil (Found: C, 67·4; H, 8·8; N, 7·4. $C_{11}H_{17}O_2N$ requires C, 67·7; H, 8·8; N, 7·2%).

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UNIVERSITY OF NOTTINGHAM. [*Received, November 17th*, 1958.]

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306. *Some New Covalent- and Ionic-halogen Derivatives of Cellobiose.*

By W. M. CORBETT and J. KIDD.

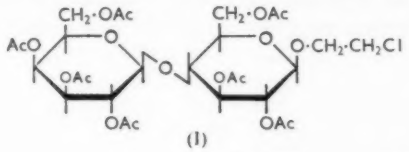
Covalent- and ionic-halogen derivatives of cellobiose have been prepared by reaction of acetobromocellobiose with 2-halogenoethanols and trimethylamine, respectively. The latter reaction has been studied in detail. The general replacement of halide by other anions in the ionic derivatives has been demonstrated.

THOUGH determination of crystal structure by *X*-ray diffraction is often aided by presence of a heavy atom, the group containing this atom should not distort the remainder of the molecule; also, the ratio of the square of the atomic number of the heavy atom to the sum of the squares of the atomic numbers of the remaining atoms should be about unity.[1] Dr. J. Mann and his collaborators of this Association are studying the crystal structure of cellulose. As a preliminary we here report the preparation and properties of heavy-atom derivatives of cellobiose.

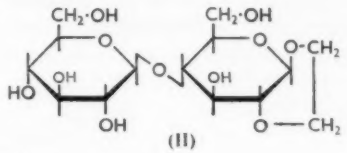
2-Chloroethyl hepta-*O*-acetyl-β-lactoside (I) was previously prepared by reaction of acetobromolactose with 2-chloroethanol.[2] Treatment of the lactoside with hot aqueous sodium hydroxide caused, not only deacetylation, but also elimination of hydrogen chloride to give an anhydride.[3] Helferich and Thiemann [4] similarly prepared 1 : 2-*O*-ethylene-β-cellobiose (II). The acetylated chloro-, bromo-, and iodo-ethyl cellobiosides and lactosides have now been prepared in a highly crystalline form, and have been catalytically deacetylated without appreciable anhydride formation. The unsubstituted glycosides were obtained crystalline, some with solvent of crystallisation. 2-Bromoethyl β-cellobioside, which otherwise would have been the most suitable derivative for study, was hygroscopic. The acetate was therefore treated with trimethylamine and deacetylated,

[1] Lipson and Cochran, "The Crystalline State. Vol. III. The Determination of Crystal Structure," Bell and Son Ltd., London, 1953, p. 207.
[2] Coles, Dodds, and Bergeim, *J. Amer. Chem. Soc.*, 1938, **60**, 1020.
[3] Helferich and Werner, *Ber.*, 1943, **76**, 595.
[4] Helferich and Thiemann, *Z. physiol. Chem.*, 1944, **281**, 126.

to give the quaternary ammonium salt (III). This compound was also hygroscopic and crystallised very poorly although ionic. Reacetylation with acetic anhydride in the presence of perchloric acid yielded the acetate perchlorate.



(I)



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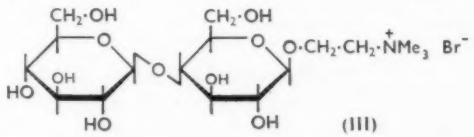
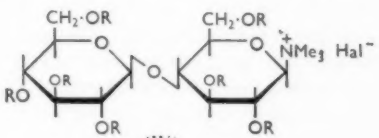
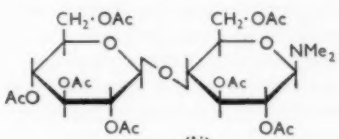


(III)

Attention was then directed to the preparation of ionic derivatives of the type (IV). Micheel and Micheel [5] observed that acetobromo-sugars in which the 2-acetyl group is *cis* to the bromine atom with trimethylamine readily give the *N*-(*O*-acetyl-β-glycosyl)trimethylammonium bromides (*e.g.*, IV; R = Ac, Hal = Br). Acetobromocellobiose appeared to react anomalously,[6] to give a product which was shown by Zemplén and Bruckner [7] to be *N*-hepta-*O*-acetyl-β-cellobiosyldimethylamine (V). The present



(IV)



(V)

reinvestigation of the reaction has shown that under certain conditions the ammonium salt is formed normally, in high yield, but readily loses methyl halide.

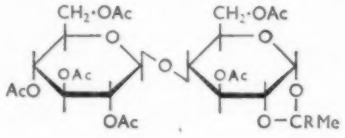
Trimethylamine and acetobromocellobiose at −180° gave an unstable compound with the same elemental analysis as the starting material, but with a lower melting point and optical rotation. Because of the sharpness of the melting point and its reproducibility, it is believed that the material consists of one component only. The melting point of the material was slowly raised by repeated recrystallisation from chloroform–light petroleum and eventually acetobromocellobiose was obtained. Thus the compound is closely related to the latter. It is well known that β-acetohalogeno-sugars are unstable and readily revert to the α-form [8] but the possibility that this new compound is β-acetobromocellobiose must be dismissed because of the high positive optical rotation. The presence of an ortho-acetate group (VI; R = Br) (cf. the similar maltose derivative obtained by Freudenberg and Ivers [9]) would explain the observed physical properties. Such a derivative would, however, be expected to give the corresponding acetate (VI; R = OAc) and ethyl derivative (VI; R = OEt) on treatment with silver acetate, and with ethanol in the presence of silver carbonate, respectively. Instead, these reactions led to β-cellobiose octa-acetate and ethyl hepta-*O*-acetyl-β-cellobioside. Finally, the possibility that the isolated compound is a crystalline modification of acetobromocellobiose is not accepted because of the difference in optical rotation. It is therefore tentatively suggested that the

[5] Micheel and Micheel, *Ber.*, 1930, **63**, 386.
[6] Zemplén, Csuros, and Bruckner, *Ber.*, 1928, **61**, 927.
[7] Zemplén and Bruckner, *ibid.*, p. 2481.
[8] Cf. Schlubach, Stadler, and Wolf, *ibid.*, p. 287; Lemieux, *Adv. Carbohydrate Chem.*, 1954, **9**, 1.
[9] Freudenberg and Ivers, *Ber.*, 1922, **55**, 929; Freudenberg, Hochstetter, and Engels, *Ber.*, 1925, **58**, 666.

XUM

compound is acetobromocellobiose of an unstable conformation. Such a change would be expected to decrease the rotation [10] and change the melting point.

The reaction of trimethylamine with a solution of acetobromocellobiose at room temperature (the conditions used by Micheel [11] for acetobromogalactose) produced *N*-hepta-*O*-acetyl-β-cellobiosyltrimethylammonium bromide (IV; R = Ac, Hal = Br) in high yield,



(VI)

together with small amounts of tetramethylammonium bromide. This product was more conveniently prepared by heterogeneous reaction of acetobromocellobiose with trimethylamine and chloroform. The quaternary bromide appeared to form a complex compound with chloroform (cf. Steinkopf *et al.*[12]). When heated, the complex melted and then resolidified, the weight loss corresponding approximately to one mol. of chloroform. The loss of chloroform was indicated by a positive test for *gem.*-polyhalides [13] before heating, and a negative test after heating. The presence of a trimethylammonium bromide group was proved by the solubility in water (despite the presence of seven acetyl groups), quantitative reaction of the bromine with silver nitrate solution, production of trimethylamine by hot alcoholic alkali, and conversion into the tertiary β-cellobiosylamine acetate (V) which with methyl bromide regenerated the ammonium salt.

A metathetical reaction in acetone between the quaternary ammonium salt and sodium iodide produced the iodide which has previously been prepared, but not isolated, by treatment of *N*-hepta-*O*-acetyl-β-cellobiosyldimethylamine with methyl iodide.[14] The chloride was obtained by chloroform extraction of an aqueous solution of the bromide containing a large excess of chloride ions. Use of a saturated solution of ammonium nitrate led to the isolation of the nitrate. The chloride, bromide, iodide, and nitrate have been catalytically deacetylated to give the respective *N*-β-cellobiosyltrimethylammonium salts in highly crystalline form.

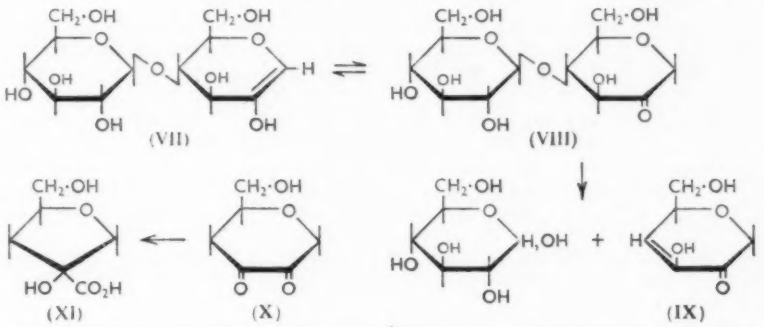
A repetition of Zemplén and Bruckner's reaction [7] at room temperature confirmed the production of *N*-hepta-*O*-acetyl-β-cellobiosyldimethylamine. Hepta-*O*-acetyl-2-hydroxycellobial was also isolated, but in low yield.

Reaction at 90° involved considerable decomposition and the major product was *N*-hepta-*O*-acetyl-β-cellobiosyldimethylamine together with tetramethylammonium bromide. A crystalline modification of the cellobiosylamine derivative was obtained in low yield. It was converted into the higher-melting, more stable form by recrystallisation and seeding. Small amounts of hepta-*O*-acetyl-2-hydroxycellobial and trimethylammonium bromide were isolated, as well as a very small quantity of an unknown compound, m. p. 214—215°, whose analysis suggested its formulation as a hexa-*O*-acetylcellobiose anhydride.

The structure of the hepta-*O*-acetyl-2-hydroxycellobial was proved by a mixed melting point with an authentic sample. However, alkaline saponification indicated the presence of eight acetyl groups. A similar phenomenon has previously been observed for tetra-*O*-acetyl-2-hydroxyglucal.[15] The titration solutions were chromatographed in basic and acidic solvents, giving indications respectively of glucose (but no other reducing component), and a non-lactonisable acid which reacted only very slowly with periodate. Thus, 2-hydroxycellobial had undergone scission at the glycosidic link to yield glucose and an

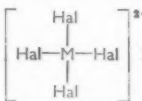
[10] Reeves and Blouin, *J. Amer. Chem. Soc.*, 1957, **79**, 2261.
[11] Micheel, *Ber.*, 1929, **62**, 687.
[12] Steinkopf and Teichmann, *J. prakt. Chem.*, 1930, **127**, 337, and previous papers.
[13] Feigl, "Spot Tests in Organic Analysis," Elsevier, Amsterdam, 1956, p. 313.
[14] Karrer and Harloff, *Helv. Chim. Acta*, 1933, **16**, 962.
[15] Maurer, *Ber.*, 1929, **62**, 332.

acid. Such a scission is readily explained by a β-alkoxycarbonyl elimination [16] as follows. Under alkaline conditions 2-hydroxycellobial (VII) is in equilibrium with 1-deoxy-2-dehydrocellobiose (VIII) in which the glucosyl group is in a position β to the carbonyl group. Elimination of the glucosyl group would leave the carbonyl-enol (IX) which would then be converted through the dicarbonyl compound (X) into the acid (XI). Since the acid contains a tetrahydrofuran ring, a second ring produced by lactonisation at the



primary hydroxyl group would impose excessive strain. The absence of a glycol group readily explains the slow oxidation by periodate.

N-Hepta-*O*-acetyl-β-cellobiosyltrimethylammonium bromide, like simple quaternary ammonium salts, forms complexes with inorganic halides,[17] *e.g.* with 0·5 mol. of calcium chloride, mercuric bromide, or mercuric iodide. These are probably co-ordination compounds. Co-ordination cannot occur through the nitrogen atoms since they bear a positive charge; moreover, the optical rotation of the organic halide is little affected by the dissolution of inorganic salt, so that it is more likely to occur by virtue of the halogen ions to give a complex of the type (XII) where Y is the cation of (IV; R = Ac). Several metal halides dissolved in a chloroform solution of *N*-hepta-*O*-acetyl-β-cellobiosyltrimethylammonium bromide, as shown in the annexed Table.



Salt	Colour of solution	M. p. of complex
$CaCl_2$	Colourless	177° (decomp.)
$CoBr_2$	Blue	140—142°
$CrCl_3$	Green	
Cu_2Cl_2	Brown	
$CuBr_2$	Purple ($CHCl_3$)	
	Yellow (MeOH)	85°
$FeCl_3$	Red-brown	
Hg_2I_2	Colourless (Hg formed)	
$HgBr_2$	Colourless	160—162°
HgI_2	Olive-green	
MgF_2	Milky	
$NiCl_2$	Blue-green	

X-Ray structural analysis of the unacetylated compounds described above is being made by Dr. W. Ferrier at the University of St. Andrews, Queen's College, Dundee.

Experimental

2-Halogenoethyl β-Cellobiosides.—(a) *2-Chloroethyl β-cellobioside.* Freshly prepared silver carbonate (2·6 g.) was added to a solution of acetobromocellobiose (3·6 g.) in 2-chloroethanol (8·8 ml.), and the mixture kept for 2½ hr. at room temperature in the dark, then for 1 hr. at 100°. The silver salts were filtered off and washed with hot ethanol; the combined filtrate and washings afforded needles (1·93 g.), m. p. 199—201°. A further crop (1·30 g.; total yield 89%) isolated from the mother-liquors had m. p. 186—198°. Several recrystallisations from ethanol gave pure 2-chloroethyl hepta-*O*-acetyl-β-cellobioside, m. p. 205—206°, $[\alpha]_D^{28}$ −8·0° (*c* 35 in

[16] Corbett and Kenner, *J.*, 1953, 2245.
[17] Amiel, *Compt. rend.*, 1935, **200**, 138; Remy and Laves, *Ber.*, 1933, **66**, 401; Remy and Meyer, *Ber.*, 1944, **77**, 679; Mellor and Quodling, *J. Proc. Roy. Soc., N.S. Wales*, 1936, **70**, 205; Mellor, *Z. Krist.*, 1939, **101**, 160.

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chloroform) (Found: C, 48·2; H, 5·5. Calc. for $C_{28}H_{39}O_{18}Cl$: C, 48·1; H, 5·6%). Helferich and Thiemann [4] give m. p. 202°, $[\alpha]_D$ −17·1°. A suspension of the acetate (2 g.) in anhydrous methanol (10 ml.) and methanolic sodium methoxide (0·6 ml.; *ca.* 0·5M) was left with occasional shaking at room temperature until dissolution was complete (3 hr.). Neutralisation with solid carbon dioxide followed by evaporation *in vacuo* yielded a yellow amorphous powder. Crystallisation from aqueous acetone yielded *2-chloroethyl β-cellobioside hemihydrate*, m. p. 213—214° (decomp.), $[\alpha]_D^{21}$ −9·5° (*c* 9·8 in water) (Found: C, 40·5; H, 6·3. $C_{14}H_{25}O_{11}Cl,\frac{1}{2}H_2O$ requires C, 40·7; H, 6·3%).

(b) *2-Bromoethyl β-cellobioside*. Acetobromocellobiose (4·4 g.) was similarly treated with 2-bromoethanol (15 ml.) and silver carbonate (3·2 g.) to yield *2-bromoethyl hepta-O-acetyl-β-cellobioside* (2·66 g., 57%), m. p. 208—211°. After recrystallisation from ethanol–acetone (1 : 1), it had m. p. 214—215·5°, $[\alpha]_D^{24}$ −11·0° (*c* 21·6 in chloroform) (Found: C, 45·1; H, 5·2; Br, 10·7. $C_{28}H_{39}O_{18}Br$ requires C, 45·2; H, 5·3; Br, 10·8%). A suspension of the acetate (1·06 g.) in methanol (5 ml.) and methanolic sodium methoxide (0·3 ml.; *ca.* 0·5M) was kept for 5 days at room temperature until dissolution was complete. A compound which separated from the neutralised solution (carbon dioxide) separated from aqueous acetone as halogen-free crystals (0·07 g.), m. p. 235—238°, depressed on admixture with cellobiose. Helferich and Thiemann [4] give m. p. 236° for 1 : 2-*O*-ethylene-β-cellobiose. Addition of ethyl acetate to the methanolic reaction solution caused the separation of hygroscopic *2-bromoethyl β-cellobioside*, m. p. 134—135° (decomp.), $[\alpha]_D^{20}$ −8·1° (*c* 4·8 in water) (Found: C, 37·4; H, 5·6. $C_{14}H_{25}O_{11}Br$ requires C, 37·4; H, 5·6%).

(c) *2-Iodoethyl β-cellobioside*. 2-Chloroethyl hepta-*O*-acetyl-β-cellobioside (2 g.), sodium iodide (2·15 g.), and acetone (15 ml.) were heated together at 85° for 6½ hr. in a sealed tube. The crystals which separated were washed with a little acetone, water (to remove sodium chloride), and finally further acetone, to give *2-iodoethyl hepta-O-acetyl-β-cellobioside* (1·22 g.), m. p. 223—224°, $[\alpha]_D^{22}$ −18·2° (*c* 21·1 in chloroform) (Found: C, 42·5; H, 4·9; I, 16·0. $C_{28}H_{39}O_{18}I$ requires C, 42·5; H, 5·0; I, 16·1%). Addition of water (150 ml.) containing a little sodium thiosulphate to the reaction solution caused further product to separate (0·41 g.; total 77%) which was recrystallised from acetone–ethanol (1 : 1).

A suspension of the acetate (1·05 g.) in methanol, deacetylated as previously described, gave in 77% yield *2-iodoethyl β-cellobioside*, m. p. 147—148°. This recrystallised with a mol. of ethyl acetate of crystallisation from methanol–ethyl acetate, then having m. p. 149—150°, $[\alpha]_D^{19}$ −12·0° (*c* 6·7 in water) (Found: C, 36·4; H, 5·5. $C_{14}H_{25}O_{11}I,C_4H_8O_2$ requires C, 37·0; H, 5·7%).

2-Halogenoethyl β-Lactosides.—2-Chloroethyl hepta-*O*-acetyl-β-lactoside was prepared in 54% yield by reaction of acetobromolactose with 2-chloroethanol as above. It had m. p. 70—75°, $[\alpha]_D^{18}$ −2·3° (*c* 1·6 in chloroform) (Found: C, 48·1; H, 5·5; Cl, 4·5. Calc. for $C_{28}H_{39}O_{18}Cl$: C, 48·1; H, 5·6; Cl, 5·1%). Coles, Dodds, and Bergeim [2] give m. p. 78—80°. Deacetylation of the acetate gave in 55% yield *2-chloroethyl β-lactoside*, m. p. 148—149° (decomp.), $[\alpha]_D^{18}$ +0·9° (*c* 3·7 in water) (Found: C, 41·1; H, 6·5; Cl, 8·3. $C_{14}H_{25}O_{11}Cl$ requires C, 41·5; H, 6·2; Cl, 8·8%).

Treatment of 2-chloroethyl hepta-*O*-acetyl-β-lactoside with sodium iodide as described for the cellobiose derivative yielded *2-iodoethyl hepta-O-acetyl-β-lactoside* (57%), m. p. 70—72°, $[\alpha]_D^{18}$ −9·4° (*c* 1·6 in chloroform) (Found: C, 42·5; H, 5·0; I, 15·3. $C_{28}H_{39}O_{18}I$ requires C, 42·5; H, 5·0; I, 16·1%). Deacetylation gave *2-iodoethyl β-lactoside* (56%), m. p. 154—155° (decomp.), $[\alpha]_D^{17}$ −2·0° (*c* 4·9 in water) (Found: C, 34·0; H, 5·3. $C_{14}H_{25}O_{11}I$ requires C, 33·9; H, 5·1%).

N-(2-β-Cellobiosyloxyethyl)trimethylammonium Bromide.—2-Bromoethyl hepta-*O*-acetyl-β-cellobioside (3 g.) and alcoholic 40% trimethylamine (*ca.* 40 ml.) were heated together at 90—95° for 1 hr. in a sealed tube, dissolution being complete after 10 min. On cooling, the yellow solution deposited colourless needles of *N-[2-(hepta-O-acetyl-β-cellobiosyloxy)ethyl]trimethylammonium bromide* (2·1 g.), m. p. 226—227° (decomp.). On recrystallising from ethanol–ether the salt was obtained as prisms, m. p. 226—227°, $[\alpha]_D^{22}$ −21·9° (*c* 10 in water) (Found: C, 46·3; H, 6·0; N, 1·7; Br, 10·0. $C_{31}H_{48}O_{18}NBr$ requires C, 46·4; H, 6·0; N, 1·8; Br, 10·0%). The salt (0·80 g.), deacetylated in the usual manner, gave deliquescent *N-(2-β-cellobiosyloxyethyl)trimethylammonium bromide* (0·33 g., 65%), m. p. 102° (decomp.), $[\alpha]_D^{20}$ −14·6° (*c* 3·1 in water) (Found: C, 39·6; H, 6·9. $C_{17}H_{34}O_{11}NBr$ requires C, 40·2; H, 6·7%). Reacetylation with acetic anhydride containing perchloric acid yielded *N-[2-(hepta-O-acetyl-β-cellobiosyloxy)ethyl]trimethylammonium perchlorate*, m. p. 180°, $[\alpha]_D^{23}$ −16·3° (*c* 0·7 in chloroform) (Found: C, 45·5; H, 5·6. $C_{31}H_{48}O_{22}NCl$ requires C, 45·3; H, 5·9%).

Reaction of Acetobromocellobiose with Trimethylamine at −180°.—Trimethylamine (*ca.* 8 g.)

cooled to −180° was added to acetobromocellobiose (5·70 g.) also cooled to −180°. The whole was allowed to attain room temperature. The residue was recrystallised from chloroform–light petroleum to give a *product* (2·82 g.), m. p. 165—180° (decomp.). Further recrystallisation from the same solvent gave long needles (1·3 g.), m. p. 157—158°, $[\alpha]_D^{21}$ +83·6° (*c* 2·0 in chloroform) (Found: C, 44·8; H, 5·2; Br, 11·7. $C_{26}H_{35}O_{17}Br$ requires C, 44·7; H, 5·1; Br, 11·5%).

The bromide (0·6 g.) was dissolved in ethanol (10 ml.) and silver carbonate added to the solution which was then kept at room temperature for 2 days. Refluxing the reaction mixture for 2 hr., and then evaporation of the solution yielded long needles of ethyl hepta-*O*-acetyl-β-cellobioside, m. p. and mixed m. p. 185—186°, $[\alpha]_D^{20}$ −21·6° (*c* 2 in chloroform).

The bromide (0·2 g.) in benzene (5 ml.) was added to silver acetate (0·12 g.), and the mixture kept at room temperature for 18 hr. with occasional shaking. It was then refluxed for 30 min., the silver salts were filtered off and washed with chloroform, and the combined filtrate and washings concentrated under reduced pressure. The residue, after recrystallisation from ethanol, had m. p. 198—199°, undepressed on admixture with an authentic sample of octa-*O*-acetyl-β-cellobiose.

Reaction of Acetobromocellobiose with Trimethylamine at Room Temperature. Isolation of N-Hepta-O-acetyl-β-cellobiosyltrimethylammonium Bromide.—To a solution of acetobromocellobiose (20 g.) in chloroform (40 ml.) at −90° was added trimethylamine (12 g.) also at −90°. After 20 hr. at room temperature crude *N-hepta-O-acetyl-β-cellobiosyltrimethylammonium bromide* (16·9 g.) was deposited. This was dissolved in the minimum of chloroform and extracted with a little water to remove a brown impurity. The aqueous washings were back-extracted with chloroform, and the combined chloroform solutions were dried ($CaCl_2$) and diluted with an equal volume of chloroform. Addition of light petroleum (b. p. 40—60°) caused the salt to crystallise as needles (13·3 g.), m. p. 178—179° (decomp.) (soften at 125°, effervesce at 130—145°, and resolidify), $[\alpha]_D^{21}$ −12·7° (*c* 1·5 in chloroform), −6·2° (*c* 11·8 in water). When heated at 78° *in vacuo* for 80 min., the crystals lost 15·3% of their weight (Calc. for $C_{29}H_{44}O_{17}NBr,CHCl_3$: $CHCl_3$, 13·8%). The salt before this treatment gave a strong positive test [13] for *gem.*-polyhalides, a weak test afterwards, and a negative test after being heated at 140° for 30 sec. Bromine remained detectable by the Beilstein test. The desolvated compound had m. p. 180—181° (decomp.) (Found: C, 45·2; H, 6·0; Br, 10·5. $C_{29}H_{44}O_{17}NBr$ requires C, 45·9; H, 5·9; Br, 10·5%).

Distillation of the solvated salt (1·5 g.) with alcoholic 2% sodium hydroxide (25 ml.) produced trimethylamine which was collected in N-hydrogen bromide (5 ml.). Evaporation of the distillate to dryness and recrystallisation of the residue from ethanol yielded colourless plates of trimethylammonium bromide (0·13 g., 47%), m. p. 258—260° (Found: Br, 57·6. Calc. for $C_3H_{10}NBr$: Br, 57·2%).

Elimination of Methyl Bromide from N-Hepta-O-acetyl-β-cellobiosyltrimethylammonium Bromide.—(a) *By triethylamine.* A solution of the solvated salt (0·75 g.) in chloroform (7 ml.) was heated with triethylamine (10 ml.) in a sealed tube at 90° for 2¾ hr. From the mixture was isolated *N*-hepta-*O*-acetyl-β-cellobiosyldimethylamine (0·08 g., 14%), m. p. 185—188°. After three recrystallisations from ethanol, the product had m. p. 210—211° (decomp.) (Found: C, 50·5; H, 5·9. Calc. for $C_{28}H_{41}O_{17}N$: C, 50·8; H, 6·2%). Zemplén and Bruckner [7] give m. p. 203°. A compound (0·015 g.) having m. p. 177—178° (decomp.), undepressed on admixture with a compound of similar melting point obtained in the normal preparation of the cellobiosylamine derivative, and starting material (0·16 g.) were also isolated.

(b) *By thermal decomposition.* The solvated salt (0·053 g.) was heated at 130—150° for 15 min. The residue (0·043 g.), recrystallised four times from ethanol, had m. p. 202—205° (decomp.), undepressed on admixture with *NN*-dimethylhepta-*O*-acetyl-β-cellobiosylamine.

N-β-Cellobiosyltrimethylammonium Bromide.—Solvated *N*-hepta-*O*-acetyl-β-cellobiosyltrimethylammonium bromide (0·6 g.) was deacetylated in the normal way. The *cellobiosylammonium salt* crystallised from methanol–acetone as plates (0·36 g., 98%), m. p. 216—217° (decomp.). Recrystallisation from water gave cubes, m. p. 219° (decomp.), $[\alpha]_D^{19}$ +6·3° (*c* 6·6 in water) (Found: C, 38·8; H, 6·3; N, 2·9; Br, 17·0. $C_{15}H_{30}O_{10}NBr$ requires C, 38·8; H, 6·5; N, 3·0; Br, 17·2%).

N-β-Cellobiosyltrimethylammonium Iodide.—A solution of sodium iodide (0·80 g.) in acetone (5 ml.) was added dropwise with stirring to a solution of the desolvated acetylated *N*-β-cellobiosyltrimethylammonium bromide (4·0 g.) in chloroform (15 ml.) and acetone (70 ml.). The solution was filtered from sodium bromide, evaporated to a small volume, diluted with chloroform, and filtered from a small amount of sodium iodide, and light petroleum (b. p. 40—60°) was added. *N-Hepta-O-acetyl-β-cellobiosyltrimethylammonium iodide* crystallised from the solution

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as needles containing one mol. of chloroform of crystallisation (4·06 g., 94%), m. p. 166° (decomp.) (effervesce at 130—150°, resolidify), $[\alpha]_D^{23}$ −13·1° (*c* 1·9 in chloroform) (Found: C, 38·7; H, 4·8. $C_{29}H_{44}O_{17}NI,CHCl_3$ requires C, 39·0; H, 4·9%). The acetate (2·0 g.) was deacetylated, to give N-β-*cellobiosyltrimethylammonium iodide* (0·99 g., 78%), m. p. 212—216° (decomp.). Addition of acetone to a concentrated aqueous solution yielded crystals of the *monohydrate*, m. p. 221° (decomp.), $[\alpha]_D^{20}$ +5·7° (*c* 8·7 in water) (Found: C, 34·0; H, 6·0. $C_{15}H_{30}O_{10}NI,H_2O$ requires C, 34·0; H, 6·1%). The anhydrous salt was obtained by heating the hydrate at 100° *in vacuo* over phosphoric oxide for 18 hr. and had m. p. 219° (decomp.) (Found: C, 35·2; H, 6·1. $C_{15}H_{30}O_{10}NI$ requires C, 35·3; H, 5·9%).

Elimination of Methyl Iodide from N-*Hepta*-O-*acetyl*-β-*cellobiosyltrimethylammonium Iodide*.—The solvated compound was heated at 130—150° for 10 min. The pale yellow residue was extracted with water, and crystallised from ethanol to give needles, m. p. 207—208° (decomp.) undepressed on admixture with *NN*-dimethylhepta-*O*-acetyl-β-cellobiosylamine.

N-β-*Cellobiosyltrimethylammonium Chloride*.—A solution of *N*-hepta-*O*-acetyl-β-cellobiosyltrimethylammonium bromide (2·5 g.) in water (5 ml.) was added to saturated aqueous sodium chloride (13 ml.). The mixture was extracted with chloroform, and the extract dried (Na_2SO_4) and concentrated under reduced pressure. Addition of light petroleum (b. p. 40—60°) caused separation of needles of N-*hepta*-O-*acetyl*-β-*cellobiosyltrimethylammonium chloride*, which, recrystallised from chloroform–light petroleum, had m. p. 192° (decomp.), $[\alpha]_D^{21}$ −5·7° (*c* 4·2 in water), −13·2° (*c* 4·5 in chloroform) (Found: C, 43·4; H, 5·7; Ionic Cl, 4·5. $C_{29}H_{44}O_{17}NCl,CHCl_3$ requires C, 43·2; H, 5·4; Ionic Cl, 4·3%). The acetate (2·0 g.) was deacetylated in the normal manner, to give N-β-*cellobiosyltrimethylammonium chloride*, m. p. 227° (decomp.), $[\alpha]_D^{22}$ +7·7° (*c* 1·5 in water) (Found: C, 42·5; H, 7·2; Cl, 8·2. $C_{15}H_{30}O_{10}NCl$ requires C, 42·9; H, 7·2; Cl, 8·5%).

N-β-*Cellobiosyltrimethylammonium Nitrate*.—A solution of the bromide (4·0 g.) in water (10 ml.) was added to saturated aqueous ammonium nitrate (40 ml.). The mixture was extracted with chloroform, and the extract dried (Na_2SO_4) and concentrated under reduced pressure. The residual syrup crystallised on trituration with ethyl acetate. The crystals (2·44 g., 60%), m. p. 205° (decomp.), were recrystallised from acetone solution by addition of ethyl acetate, giving needles of N-*hepta*-O-*acetyl*-β-*cellobiosyltrimethylammonium nitrate* containing ethyl acetate of crystallisation, m. p. 208° (decomp.), $[\alpha]_D^{21}$ −6·8° (*c* 6·5 in water). After removal of ethyl acetate at 78° over phosphoric oxide, the material had m. p. 202° (decomp.) (Found: C, 46·6; H, 6·0. $C_{29}H_{44}O_{20}N_2$ requires C, 47·0; H, 6·0%). The acetate was deacetylated in the normal manner to give N-β-*cellobiosyltrimethylammonium nitrate*, m. p. 215° (decomp.), $[\alpha]_D^{20}$ +7·5° (*c* 9·7 in water) (Found: C, 40·0; H, 7·0. $C_{15}H_{30}O_{13}N_2$ requires C, 40·4; H, 6·8%).

Reaction of Acetobromocellobiose with Trimethylamine at Room Temperature. Isolation of N-*Hepta*-O-*acetyl*-β-*cellobiosyldimethylamine*.—Trimethylamine (3·0 g.) was added to acetobromocellobiose (10 g.) in chloroform (40 ml.), kept at room temperature for 16 days with occasional shaking, and then evaporated, and the resulting residue crystallised twice from ethanol to give *N*-hepta-*O*-acetyl-β-cellobiosyldimethylamine (4·16 g., 44%), m. p. 207—209° (decomp.). Zemplén and Bruckner [7] give m. p. 203°. Addition of water to the ethanol mother-liquors gave hepta-*O*-acetyl-2-hydroxycellobial as plates, which after two recrystallisations from ethanol had m. p. and mixed m. p. 127—128° (0·55 g., 6%).

Reaction of Acetobromocellobiose with Trimethylamine at 90°.—Ethanolic trimethylamine (*ca.* 40%; 80 ml.) and acetobromocellobiose (10 g.) were heated at 85—95° for 2 hr. The white crystals produced were fractionally crystallised, to give, as the main product, *N*-hepta-*O*-acetyl-β-cellobiosyldimethylamine (2·72 g., 29%), m. p. 210—211° (decomp.), $[\alpha]_D^{21}$ −11·5° (*c* 2·9 in chloroform) (Found: C, 50·7; H, 6·1; N, 1·9; Ac, 45·8. Calc. for $C_{28}H_{41}O_{17}N$: C, 50·8; H, 6·2; N, 2·1; Ac, 45·4%). Zemplén *et al.*[6] give m. p. 205° (decomp.), $[\alpha]_D^{20}$ −11·5° (in chloroform). Distillation of the product (0·45 g.) with alcoholic 2% sodium hydroxide (15 ml.) and collection of the distillate in hydrogen bromide gave needles of dimethylammonium bromide (0·04 g., 47%), m. p. *ca.* 150° (Found: Br, 63·9. Calc. for C_2H_8NBr: Br, 63·5%). A sample (0·10 g.) was heated in methyl bromide (*ca.* 1 g.) at 100° for 5 min., then cooled to room temperature during 2 hr. Excess of methyl bromide was evaporated and the residue crystallised from chloroform–light petroleum (b. p. 40—60°), to give needles (0·07 g., 44%) of *N*-hepta-*O*-acetyl-β-cellobiosyltrimethylammonium bromide, m. p. 180° (effervesce at 80°, resolidify at 150°), undepresed on admixture with the previously prepared salt.

From the mother-liquors were also isolated (*a*) tetramethylammonium bromide (1·04 g., 47·5%) (Found: Br, 52·0. Calc. for $C_4H_{12}NBr$: Br, 52·0%), (*b*) trimethylammonium bromide (0·01 g., 0·5%) (Found: Br, 57·5. Calc. for $C_3H_{10}NBr$: Br, 57·2%), (*c*) a compound (0·19 g.), m. p. 177—178° (decomp.), $[\alpha]_D^{22}$ −11·7° (*c* 0·2 in chloroform) (Found: C, 50·9; H, 6·5; N, 2·1. Calc. for $C_{28}H_{41}O_{17}N$: C, 50·8; H, 6·2; N, 2·1%), which was a lower-melting form of *N*-hepta-*O*-acetyl-β-cellobiosyldimethylamine. Recrystallisation from ethanol and seeding with the higher-melting form gave the higher-melting form, m. p. and mixed m. p. 209—210° (decomp.), (*d*) an unidentified halogen- and nitrogen-free compound (0·04 g.), m. p. 214—215° (Found: C, 49·6; H, 5·6%), and (*e*) hepta-*O*-acetyl-2-hydroxycellobial (0·35 g., 4%), m. p. and mixed m. p. 128—129° (Found: C, 50·5; H, 5·4. Calc. for $C_{26}H_{34}O_{17}$: C, 50·6; H, 5·6%).

Hepta-*O*-acetyl-2-hydroxycellobial (0·0686 g.) in dioxan (5 ml.) was saponified with 0·01N-sodium hydroxide (10 ml.) at room temperature for 80 min. Alkali consumed was 7·90 equiv. An authentic sample under similar conditions consumed 7·80 equiv. The titration solution was stirred with Amberlite Resin IR-120(H), filtered, stirred with barium carbonate, filtered, again stirred with resin, filtered, and concentrated. Chromatography of the resultant syrup in ethyl acetate–pyridine–water (8 : 2 : 1) revealed the presence of glucose, and in ethyl acetate–acetic acid–water (10 : 1·3 : 1) an acid with R_{Lactic} 0·51 was detected with "B.D.H. 4·5" indicator spray.[18] It slowly reacted with permanganate–periodate spray,[19] and gave no reaction with hydroxylamine–ferric chloride spray for lactones.[20]

Reaction of N-*Hepta*-O-*acetyl*-β-*cellobiosyltrimethylammonium Halides with Inorganic Salts.* —(a) *Calcium chloride.* A solution of calcium chloride (30 g.) in water (20 ml.) was added to one of *N*-hepta-*O*-acetyl-β-cellobiosyltrimethylammonium bromide (5 g.) in water (10 ml.), and the mixture was extracted with chloroform (6 × 50 ml.). The chloroform extracts were dried ($CaCl_2$), concentrated under reduced pressure to 100 ml., and diluted with light petroleum (b. p. 40—60°; *ca.* 40 ml.). The solution yielded hygroscopic needles (4·1 g.) of a *complex*, m. p. 170° (decomp.). Recrystallised from chloroform–light petroleum (b. p. 40—60°) this had m. p. 177° (decomp.) (effervesces at 150°; resolidifies), $[\alpha]_D^{22}$ −12·2° (*c* 5·7 in chloroform) (Found: Ionic Cl, 8·1; Ca, 2·2. $C_{28}H_{44}O_{17}NCl,CHCl_3,\frac{1}{2}CaCl_2$ requires Ionic Cl, 8·0; Ca, 2·3%).

(b) *Mercuric bromide.* Solid mercuric bromide (0·21 g.), added to a solution of *N*-hepta-*O*-acetyl-β-cellobiosyltrimethylammonium bromide–chloroform complex (0·50 g.) in chloroform (3 ml.), dissolved at room temperature in a few seconds. The solution was filtered from the slight excess of mercuric bromide and evaporated under reduced pressure. The residue crystallised from hot absolute methanol (15 ml.) as prisms (0·37 g.), m. p. 160—162°, $[\alpha]_D^{21}$ −8·7° (*c* 9·0 in chloroform). To estimate the bromine present, a solution of the *complex* (0·252 g.) in acetone (2·5 ml.) was treated dropwise with sodium iodide in acetone (5%; 2 ml.) and kept for 10 min. at room temperature. The sodium bromide precipitated was filtered off, washed with acetone, and titrated in aqueous solution against silver nitrate (Found: Br, 15·4. $C_{28}H_{44}O_{17}NBr,CHCl_3,\frac{1}{2}HgBr_2$ requires Br, 15·2%). The acetone filtrate from the sodium bromide precipitate was concentrated, diluted with chloroform to precipitate excess of sodium iodide, filtered, and concentrated under reduced pressure to a green syrup which crystallised from hot absolute methanol as yellow-green needles, m. p. 184—185°, undepressed on admixture with the iodide compound described below.

(c) *Mercuric iodide.* Red mercuric iodide (0·33 g.) was dissolved in a solution of *N*-hepta-*O*-acetyl-β-cellobiosyltrimethylammonium iodide–chloroform complex (0·66 g.) in chloroform (3 ml.). The olive-green solution was worked up in the same way as in the mercuric bromide experiment, the product crystallising from hot absolute methanol as yellow-green needles, m. p. 183° (sinter at 180°).

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307. *Polarography of Iodide and Chloride Ions in Dimethylformamide.*

By P. H. Given and M. E. Peover.

Polarograms of iodide or chloride ion with a dropping mercury electrode in dimethylformamide show two anodic waves, of which that at the more negative potential is due to the oxidation of mercury to the tetrahalogenomercurate ion. The waves become cathodic on addition of mercuric perchlorate. The overall equilibrium constant for the reaction $Hg^{2+} + 4I^- \rightleftharpoons HgI_4^{2-}$ is approximately $6{\cdot}2 \times 10^{29}$ at 20° in 0·1M-lithium perchlorate. Mercurous chloride is soluble in solutions of lithium chloride in dimethylformamide. The use of a mercury pool anode as a reference electrode in polarography in halide–dimethylformamide solutions is discussed in the light of these results.

Various polarographic studies [1-5] have indicated that the potential of a mercury anode under a solution of tetra-alkylammonium iodide in dimethylformamide (and probably also in dioxan–water, acetonitrile, and Methyl Cellosolve) assumes a well-regulated value, suitable for reference purposes. This potential is in each case some 0·5 v negative to an aqueous saturated calomel electrode. We report here experiments designed to elucidate some features of the chemistry of mercury relating to these facts. A note describing some of the results has appeared.[6]

Experimental

Dimethylformamide was as received from Griffin and George; the water content (Karl Fischer) was about 0·01%. Tetraethylammonium iodide was prepared as described previously.[2]

Other materials were " AnalaR " if available, or otherwise a good laboratory grade. However, mercuric perchlorate was used as a concentrated aqueous solution, made by neutralising 60% perchloric acid with solid mercuric oxide. A Tinsley polarograph, model 14/3, was used for the polarographic measurements. An H-cell was used for polarography; the bridge liquid, separated from the calomel and polarographic cells by No. 4 porosity sintered-glass discs, consisted of 1·0N-aqueous lithium perchlorate, and the base solution for polarography was a 0·1N-solution of the same salt in dimethylformamide. In some experiments the bridge solution was made up in dimethylformamide instead of water. This was found to be unsatisfactory because potassium chloride from the calomel cell crystallised on the sinter in the organic solvent; this made the cell resistance and measured potentials variable. All the results were corrected for *iR* drop. The anode-to-cathode resistance was 1500—4000 ohms.

Conductivities were measured with a Mullard conductivity bridge, operated at 3kc./sec., and blacked platinum electrodes.

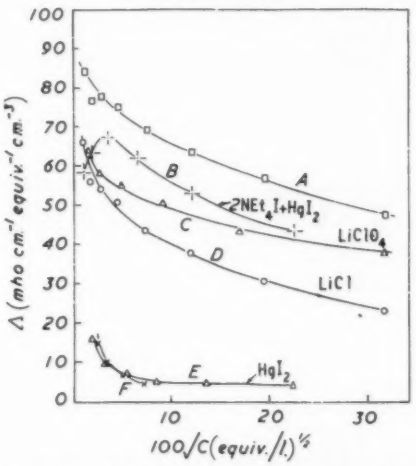
Results.—(a) *Solubility relations.* Mercuric chloride, iodide, and perchlorate, lithium chloride and perchlorate, and a number of tetra-alkylammonium salts were easily soluble in dimethylformamide, and mercurous chloride and iodide are insoluble (mercuric iodide is extremely soluble: *ca.* 4M at 20°). A solution of mercuric chloride in dimethylformamide shaken with mercury at once precipitates the mercurous compound, but if 0·1N-lithium chloride or tetraethylammonium iodide is present, no precipitation occurs. If calomel is shaken with lithium chloride solution for some while, it dissolves and mercury separates; on dilution with water the solution gives positive reactions for Hg^{II} (H_2S, dithizone). Lithium perchlorate does not prevent separation of calomel from a solution of mercuric chloride containing mercury. There is little separation of mercurous iodide when a solution of the mercuric salt in dimethylformamide is shaken with mercury.

[1] Hoijtink, van Schooten, de Boer, and Aalbersberg, *Rec. Trav. chim.*, 1954, **73**, 355.
[2] Given, Peover, and Schoen, *J.*, 1958, 2674.
[3] Wawzonek, Blaha, Berkey, and Runner, *J. Electrochem. Soc.*, 1955, **102**, 235.
[4] Bergmann, *Trans. Faraday Soc.*, 1954, **50**, 829; 1956, **52**, 690.
[5] Given, *J.*, 1958, 2685.
[6] Given and Peover, *Nature*, 1958, **182**, 1226.

(b) *Conductivities.* A few approximate measurements of the conductivity of solutions of some salts in dimethylformamide have been made, to test the ionisation of mercuric compounds in this medium. The equivalent conductivities at room temperature (about 20°) are plotted in Fig. 1, together with those of the supporting electrolytes for comparison; the conductivity of a mixture of tetraethylammonium iodide and mercuric iodide of mole-ratio 2 : 1 is also shown.

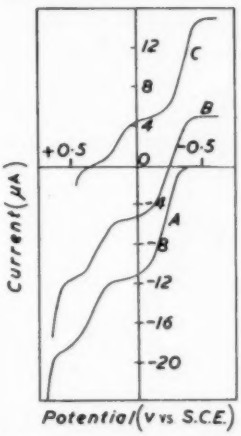
(c) *Polarographic measurements.* The nature of the reactions of mercury in the polarographic cell has been investigated by studying the polarography of lithium chloride and tetraethylammonium iodide in 0·1N-lithium perchlorate as supporting electrolyte, with and without added mercuric ions. A similar study of these system in aqueous solutions has been made by Kolthoff and Miller,[7] and we followed their methods.

FIG. 1. *Equivalent conductivities of salts in dimethylformamide.*



A, NEt_4I. *B*, Conductivity and concentration of the mixture $2NEt_4I + HgI_2$, calculated on the basis of complete association to $(NEt_4)_2HgI_4$. *C*, $LiClO_4$. *D*, LiCl. *E*, HgI_2. *F*, $HgCl_2$.

FIG. 2. *Polarography of tetraethylammonium iodide in 0·1M-lithium perchlorate.*



A, 4·76mM. *B*, 4·76mM-NEt_4I + 0·7mM-$Hg(ClO_4)_2$. *C*, 4·76mM-NEt_4I + 2·1mM-$Hg(ClO_4)_2$.

Lithium perchlorate by itself gave a "dissolution wave," that is, the current increased without limit as the potential of the dropping mercury electrode become more positive (above +0·4 v). Perchlorates in aqueous solutions give a similar wave,[6] owing to the reaction $2Hg \longrightarrow Hg_2^{2+} + 2e$, and the equation of the wave is $E_{de} = E_{Hg}^{\circ} + (RT/2F) \ln i$. Plots of E_{de} against log i for lithium perchlorate in dimethylformamide gave fairly good straight lines of slopes 0·03—0·045 v (this type of plot is exceptionally sensitive to errors in the measurement of potential and the correction for iR drop).

TABLE 1. *Polarography of iodide and chloride ions in 0·1N-lithium perchlorate in dimethylformamide.*

Salt	Concn. (mM)	$E_{\frac{1}{2}}$ (v *vs.* S.C.E.)	I	Temp.
LiCl	2·52	−0·17, +0·125	1·17, 0·52	19·5°
NEt_4I	1·96	−0·32, +0·10	1·24, 0·50	20

Lithium chloride and tetraethylammonium iodide in 0·1N-lithium perchlorate both give two oxidation waves (see example in Fig. 2, *A*), whose half-wave potentials and wave heights, I ($= i_d/cm^{\frac{2}{3}}t^{\frac{1}{6}}$), are given in Table 1. The wave heights were effectively constant in the concentration range 1—5mM; average values are given in Table 1.

[7] Kolthoff and Miller, *J. Amer. Chem. Soc.*, 1941, **63**, 1403.

In the analysis of the waves of complex mercury ions used by Kolthoff and Miller [7] one writes the electrode reaction as:

$$Hg + aX^- \rightleftharpoons HgX_a^{(a-2)-} + 2e \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

The potential of the dropping electrode is given by:

$$E_{de} = C + (\boldsymbol{R}T/2\boldsymbol{F}) \ln [Hg^{2+}] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where $[Hg^{2+}] = K[HgX_a^{(a-2)-}]/[X^-]^a$ and C is a constant.

It can easily be shown that the equation of the wave is

$$E_{de} = C' + (\boldsymbol{R}T/2\boldsymbol{F}) \ln [i/(i_d - i)^a] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Hence one plots E_{de} against the logarithmic function for various values of a, to determine the value that gives a straight line of slope $\boldsymbol{R}T/2\boldsymbol{F}$. A plot of E_{de} against $\log i/(i_d - i)^4$ for the more

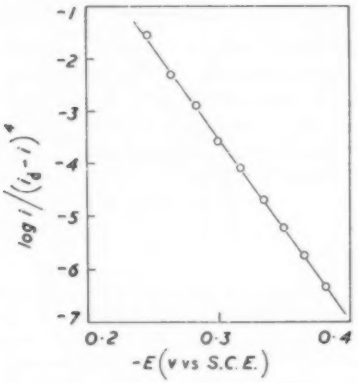


FIG. 3. *Logarithmic analysis of more negative wave of* 4·76mM-*tetraethylammonium iodide in* 1·0M-*lithium perchlorate–dimethylformamide* (*slope* 0·029v).

negative iodide wave gives a good straight line of slope 0·029 (see Fig. 3), and the electrode reaction is therefore:

$$Hg + 4I^- \rightleftharpoons HgI_4^{2-} + 2e \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

The corresponding plot for the more negative chloride wave was linear with about the required slope over the greater part of its length but became curved at less negative values of E_{de}, suggesting complication by a further reaction:

$$HgCl_4^{2-} \rightleftharpoons HgCl_3^- + Cl^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

Equation (3) shows that the half-wave potentials should be concentration-dependent:

$$E_{\frac{1}{2}} = C'' - (3\boldsymbol{R}T/2\boldsymbol{F}) \ln i_d \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

that is, a ten-fold increase in concentration should shift $E_{\frac{1}{2}}$ to more negative potentials by 0·09 v. In the range of concentrations studied (1—5 mM) the shift appeared to be less than would correspond with this for the iodide wave and more for the chloride wave.

For reasons set out in the Discussion Kolthoff and Miller's analysis cannot be applied to the more positive halide waves and we have not succeeded in identifying the electrode reactions. The unexpected observation was made that the half-wave potential of the iodide wave became more *positive* with increasing concentration.

As increasing amounts of mercuric perchlorate were added to solutions of lithium perchlorate containing definite amounts of a halide ion both waves became cathodic and finally with sufficient Hg^{2+} the "dissolution wave" became partly cathodic (see Fig. 2, *B* and *C*); at the same time the waves decreased somewhat in height, which is consistent with the lower diffusion coefficient of the complex ions compared with ligand. The shape of the more negative waves, and in 1·95mM-iodide and 3·7mM-chloride the half-wave potentials, was unchanged by additions of mercuric perchlorate up to 2mM. In 4·76mM-iodide there was an appreciable shift of both

half-wave potentials to more negative voltages as mercuric ion was added. We do not attempt to correlate the ratio of cathodic to anodic parts of the wave with amount of mercuric perchlorate added, since the concentration of the latter, owing to its method of preparation, was not known accurately.

(d) *Stability constants of complex mercuric ions.* The standard procedure [8] for determining polarographically the stability constants of complex metal ions cannot be applied to the oxidation waves of mercury complexes,[9] and special procedures have to be used. We followed the method used by Nyman, Roe, and Masson [9] in their study of ethylenediamine complexes of mercury. This requires the measurement, not of half-wave potentials, but of the potential at which the current is 1 μA more negative than the residual current. If the potentials, defined in this way, are E'_s and E'_c for the simple and complex ions respectively, then

$$E'_c = E'_s - (\boldsymbol{RT}/n\boldsymbol{F}) \ln \beta_a (C f_{X^-})^a \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

where β_a is the overall equilibrium constant of the formation of the complex HgX_a, and C is the concentration and $f_{x'}$ the activity coefficient of the complexing agent; it is assumed in this equation that the ratio of the square roots of the diffusion coefficients of complex ion to ligand

FIG. 4. *Difference in potentials of simple and complex mercuric ions as a function of concentration of tetraethylammonium iodide (slope 0·116v).*

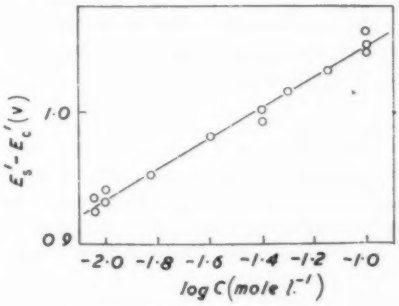
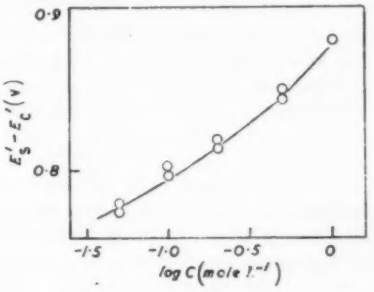


FIG. 5. *Difference in potentials of simple and complex mercuric ions as a function of concentration of lithium chloride.*



is unity. In using this method the concentration of complexing agent must be high enough for the concentration on the electrode surface to be effectively equal to that in the bulk of the liquid. For a complex HgX_4^{2-} eqn. (7) can be rewritten:

$$E'_s - E'_c = (\boldsymbol{RT}/2\boldsymbol{F}) \ln \beta_4 + (2\boldsymbol{RT}/\boldsymbol{F}) \ln f_{X^-} + (2\boldsymbol{RT}/\boldsymbol{F}) \ln C \quad . \quad . \quad . \quad (8)$$

Thus in a solution of constant ionic strength, where f_{X^-} will be constant, a plot of $E'_s - E'_c$ against log C should give a straight line of slope 0·116 at 20°. Since the potential, E''_s, measured on the dissolution wave refers to mercurous ion, it is necessary, in order to obtain E'_s, to add to E''_s the difference between the standard electrode potentials of the mercury–mercuric and mercury–mercurous couples (0·06 v).

We have measured the potentials, E'_c and E''_s, for tetraethylammonium iodide solutions of concentration 0·01—0·1M at 20°, keeping the total ionic strength at 0·1M by additions of lithium perchlorate. The results are shown in Fig. 4; it is seen that a good straight line of the theoretical slope for the HgI_4^{2-} complex is obtained. From the intercept at $C = 1$, we obtain the product $\beta_4 f_{I^-}^{-4} = 6{\cdot}5 \times 10^{28}$ for a total ionic strength of 0·1M at 20°. A few similar measurements were made for chloride ion in the range 1—0·04M, the total ionic strength being kept at 1·0M by additions of lithium perchlorate, with results shown in Fig. 5. Here a curve is obtained showing that appreciable amounts of more than one complex exist at equilibrium at these concentrations. The tangent to the curve at log $C = 0$ has approximately the slope required for the $HgCl_4^{2-}$ complex.

[8] Kolthoff and Lingane, "Polarography," Interscience, New York, 2nd Edn. 1952, p. 211 *et seq.*
[9] Nyman, Roe, and Masson, *J. Amer. Chem. Soc.*, 1955, **77**, 4191.

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Overall thermodynamic equilibrium constants for the formation of the mercuric complexes were calculated from the above data by the graphical method of de Ford and Hume;[10] this in effect uses extrapolation to zero concentration of complex, so that knowledge of activity coefficients is unnecessary. The data permitted calculation of β_2, β_3, and β_4 for iodide complexes and an approximate value of β_4 for the chloride case (see Table 2).

Discussion

The very high solubility of mercuric iodide suggested the possibility of autocomplex formation, one or both ions perhaps being solvated. However the low degree of ionisation shown by the conductivity measurements argues against this. The data for none of the salts fit the Onsager equation, and plots of Λ_C against $1/\Lambda$ (not shown) demonstrate that the Ostwald equation is not obeyed. These deviations, indicating ion-pair formation and higher degrees of ionic association, seem suprising in a solvent of fairly high dielectric constant (36·7 at 25°). The decrease in conductivity of the mixture of mercuric and tetraethylammonium iodides at low concentration suggests that dissociation of the HgI_4^{2-} complex to a lower complex occurs in very dilute solution.

The solubility relations among the chlorides of mercury evidently differ in dimethylformamide. The behaviour in the presence of excess of chloride depends on the equilibrium:

$$Hg_2Cl_2(s) + Cl^- \rightleftharpoons Hg(l) + HgCl_3^-$$

(or the corresponding reaction involving $HgCl_4^{2-}$). The observations recorded above show that the equilibrium lies much further to the right in dimethylformamide than in water and the potential of a mercury pool in chloride–dimethylformamide solution cannot be determined by the calomel equilibrium:

$$2Hg + 2Cl^- \rightleftharpoons Hg_2Cl_2(s) + 2e$$

The polarographic characteristics of the more negative iodide wave show that in polarography with iodide supporting electrolyte and a mercury pool as anode the metal goes into solution, yielding HgI_4^{2-} ions. Thus the potential of the anode is determined by the oxidation–reduction system of reaction (4); its value remains constant presumably because stable complex formation maintains a concentration of mercury ions in the anode layer sufficiently high to ensure that further quantities, produced by electrolysis, do not increase it by a significant fraction. The similarity of the half-wave potentials of hydrocarbons with iodide supporting electrolyte in dimethylformamide, 75% and 96% dioxan–water, acetonitrile, and Methyl Cellosolve (see ref. 5) creates the presumption that the pool potential is similar in all these media and therefore that the same equilibrium determines it.

Table 2. *Equilibrium constants of formation of complex mercuric ions (data for systems in water and acetonitrile taken from ref.* 12).

Ligand	Medium	log K_3	log K_4	log β_4	log K_3K_4
Cl^-	0·5M-$NaClO_4$–H_2O	0·95	1·05	15·22	2·0
Cl^-	CH_3·CN	6·0	2·23	—	8·23
Cl^-	1·0M-$LiClO_4$–DMF *	—	—	*ca.* 30	—
I^-	0·5M-$NaClO_4$–H_2O	3·67	2·37	29·86	6·04
I^-	CH_3·CN	5·95	1·61	—	7·56
I^-	0·1M-$LiClO_4$–DMF *	4—5	2·79	38·79	*ca.* 7

* DMF = Dimethylformamide: measurements made at 20°.

We have found that a mercury pool used as anode in perchlorate does not provide a stable reference potential; for example the first half-wave potential of anthraquinone is concentration-dependent in perchlorate solution but not in iodide or chloride. The potential of the pool in 0·1M-lithium perchlorate is about −0·28 v *vs.* S.C.E. and +0·3 v *vs.* mercury pool in 0·1M-tetraethylammonium iodide. Brown and Al-Urfali[11] have reported

[10] de Ford and Hume, *ibid.*, 1951, **73**, 5321.
[11] Brown and Al-Urfali, *J. Amer. Chem. Soc.*, 1958, **80**, 2113.
[12] Stability Constants of Metal-ion Complexes. Part II. Chem. Soc. Special Publ. No. 7, 1958.

the half-wave potentials of a number of metal ions each at a single concentration in dimethylformamide, referred to the potential of the pool. For some ions they used an iodide as supporting electrolyte and for others a perchlorate; they appear not to have appreciated that the reference potentials are considerably different in these media or to have considered their stability.

The stability constants of the complex mercury ions are higher (in the case of chloride as ligand, much higher) in dimethylformamide than they are in water. Some comparative figures for solutions in water and in acetonitrile (in which the constants are also higher than they are in water) are collected in Table 2; the notation used is that of the source of the data,[12] that is, the β's are overall constants, and the K's refer to addition of one ion of ligand.

It is primarily these differences in stability constants that cause much of the familiar solution chemistry of mercury to be considerably changed if dimethylformamide is used as solvent.

It is noteworthy that the pool potential in 0·1N-tetraethylammonium iodide and in 1·0N-lithium chloride in dimethylformamide is close to the electrocapillary maximum of mercury.[2] Consequently the drop-time is the same whether the electrodes are in open or short circuit.

We suggest that the more positive wave given by both halides arises as follows. As the potential of the dropping electrode is made more positive starting from, say, −0·4 V, mercury goes into solution by reaction with halide ions. At the more positive end of the first wave the halide concentration on the drop is zero, and all halide ions arriving at it by diffusion react to give HgX_4^{2-} (which in the case of chloride may dissociate to some extent to $HgCl_3^-$). However, at a sufficiently positive potential, the oxidation of mercury to another complex, perhaps HgX_3^-, becomes possible, and as the potential traverses this second wave the ratio HgX_3^-/HgX_4^{2-} on the drop increases until at the more positive end all the halide reacts to give the second complex only. The shape of the wave is therefore governed by *two* equilibria, the stationary concentration of halide on the drop being zero throughout. We have not succeeded in setting up the equation of this complex wave; the suggestion that it characterises oxidation to trihalogenomercurate is plausible but not proved.

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308. *The Birch Reduction of Some Substituted Octahydro-2-hydroxy-12-methylphenanthrenes.*

By F. H. HOWELL and D. A. H. TAYLOR.

Reduction of derivatives of 1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydro-2-hydroxy-12-methylphenanthrene with sodium and methanol in liquid ammonia proved disappointing. The expected products of addition of two hydrogen atoms were obtained, but the parent compound was extremely difficult to reduce, while the more reactive 6- and 7-methoxylated derivatives gave small yields, as the methoxy-group was also lost.

REDUCTION of *trans*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydro-2β-hydroxy-12-methylphenanthrene * (II) or, more conveniently, the unsaturated ketone 2 : 3 : 4 : 9 : 10 : 12-hexahydro-12-methyl-2-oxophenanthrene (I) with 100 equivalents of sodium in methanol and

* The stereochemical nomenclature used in this paper is as follows: *trans* and *cis* refer to the 11 : 12-ring-junction positions; α and β are used in the steroid sense with the 12-methyl group arbitrarily considered as β. All the compounds recorded are optically inactive, and formulæ and names should be held to include the mirror images.

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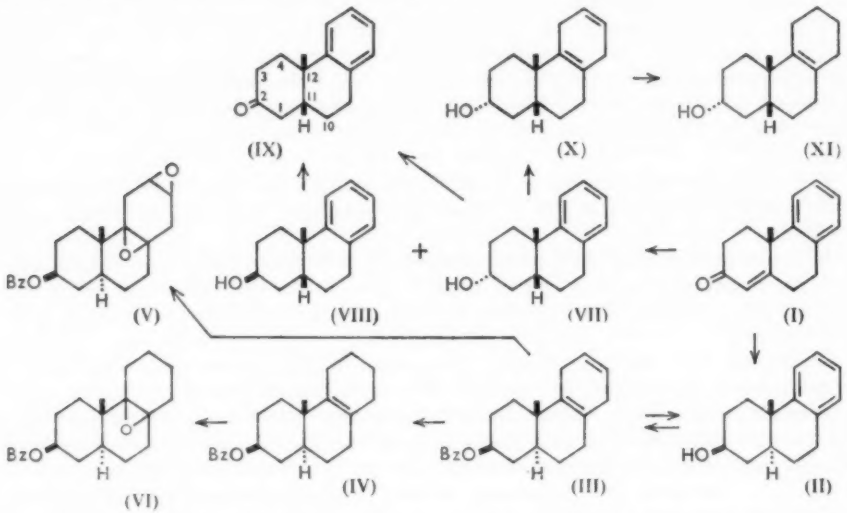
liquid ammonia gave 72% of *trans*-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10 : 11 : 12-decahydro-2β-hydroxy-12-methylphenanthrene, isolated as its crystalline benzoate (III). A smaller amount of sodium left unchanged starting material. The use of lithium in place of sodium was unsatisfactory as an insoluble lithium salt separated.



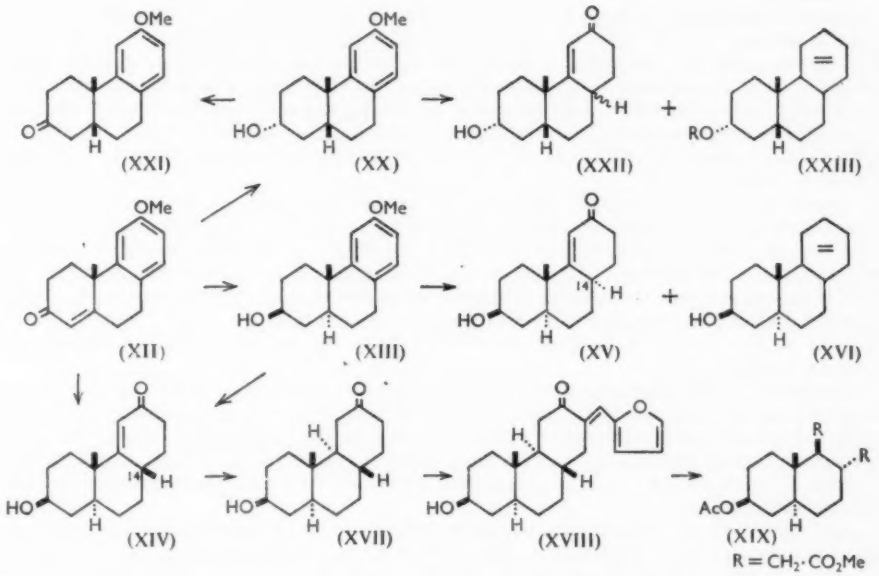
Addition of two hydrogen atoms at the unsubstituted *para*-position of an aromatic ring as in (III) is usual in a Birch reduction, and the structure is supported by the reactions of the compound, and by the fact that the free alcohol showed no selective ultraviolet absorption. Permanganate oxidation of the benzoate (III) gave the benzoate of the original alcohol (II), and performic acid gave a diepoxide (V). On hydrogenation over palladised calcium carbonate, compound (III) took up one mol. of hydrogen, giving *trans*-2β-benzoyloxy-1 : 2 : 3 : 4 : 5 : 6 : 7 : 8 : 9 : 10 : 11 : 12-dodecahydro-12-methylphenanthrene (IV). This was unaffected by permanganate, but gave an epoxide (VI) with performic acid. On hydrogenation of the benzoate (IV) over Adams catalyst in acetic acid, only the phenyl group was reduced, giving the hexahydrobenzoate of the same alcohol. Ozonolysis of the decahydrobenzoate gave a compound which cyclised on working up, and the product was a carbonyl compound $C_{22}H_{24}O_3$, giving a dark red dinitrophenylhydrazone and having an absorption maximum at 1677 cm.$^{-1}$. The preparation was difficult to repeat, and we have no evidence to show which of the double bonds was split in this reaction.

Hydrogenation of the unsaturated ketone (I) over Raney nickel gave both 2α- and 2β-*cis*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydro-2-hydroxy-12-methylphenanthrene (VII) and (VIII); each is oxidised to the amorphous *cis*-ketone (IX). Birch reduction of the more plentiful 2α-hydroxy-compound (VII) was similar to that of the *trans*-isomer (II), the deca- and dodecahydro-phenanthrenes (X) and (XI) being obtained.

Reduction of *trans*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydro-2β-hydroxy-6-methoxy-12-methylphenanthrene (XIII) or the related unsaturated ketone (XII) with 30 equivalents of lithium or sodium in methanol and liquid ammonia gave, after acid hydrolysis, a crystalline unsaturated ketone, $C_{15}H_{22}O_2$, in about 20% yield. The usual course of Birch reduction would produce one of the isomers (XIV) or (XV), which fit the analytical data. We consider that epimerisation during the acid-treatment will yield a larger amount of the isomer in which the 14-hydrogen atom is *cis* to the angular methyl group, and we provisionally assign to this product the structure (XIV). The mother-liquors gave 4% of an isomer (isolated as its benzoate) to which we assign formula (XV). The remainder of

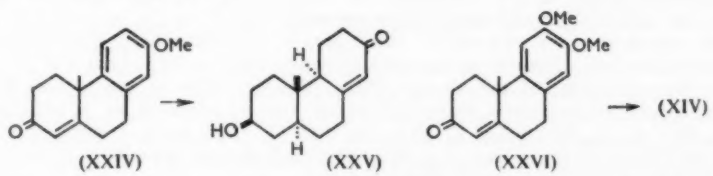
the reaction product was non-ketonic, and from it one crystalline compound (XVI) has been isolated. This contains one double bond, but is not identical with the isomer (alcohol from IV) obtained previously. It was not hydrogenated over palladised calcium carbonate, but over Adams catalyst in acetic acid gave the hexahydrobenzoate of a fully saturated alcohol. There is no evidence of the location of the double bond in this compound.

Further reduction of the unsaturated ketone (XIV) with sodium in liquid ammonia, or better hydrogenation over palladised calcium carbonate, gave a saturated ketone which we



consider to be the all-*trans*-isomer (XVII). This was not obtained entirely pure, for neither the benzoate nor the free alcohol was sharp-melting, and the dinitrophenylhydrazone was amorphous. With furfuraldehyde it gave the derivative (XVIII), which on ozonolysis gave a diacid, isolated as the crystalline acetate dimethyl ester (XIX).

Hydrogenation of the ketone (XII) over Raney nickel gave *cis*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydro-2α-hydroxy-6-methoxy-12-methylphenanthrene (XX). This was oxidised to the *cis*-ketone (XXI). Reduction of the *cis*-alcohol (XX) was similar to that of the *trans*-isomer, and gave a small yield of an unsaturated ketone (XXII) with, mostly, non-ketonic products from which an unsaturated benzoate (XXIII; R = Bz) was isolated. The location of the double bond in this compound is unknown, as is the full stereochemistry of the ketone (XXII).



Reduction of the ether (XXIV) gave a similar low yield of an unsaturated ketone, whose analysis agrees with the expected formula (XXV). We have also investigated the

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reduction of the diether (XXVI): it gave a mixture from which only the ketone (XIV) was isolated.

Earlier we described[1] the ring extension of 1-methyl-2-tetralone by alkylation with 4-chlorobutan-2-one. This method, due to Walker,[2] has now been extended to the methoxy-derivatives. Uniformly good yields are obtained under suitable conditions. The preparation of the 6-methoxy-compound (XII) in this way is described below.

Experimental

trans-2β-*Benzoyloxy*-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10 : 11 : 12-*decahydro*-12-*methylphenanthrene* (III).—To a solution of 2 : 3 : 4 : 9 : 10 : 12-hexahydro-12-methyl-2-oxophenanthrene (I) (1·0 g.) in dry methanol (100 ml.) and liquid ammonia (180 ml.) was added sodium (10 g.) in pieces during 20 min. After evaporation of the ammonia, water and ether were added, and the ether layer was washed and evaporated. Benzoylation of the residue and crystallisation from ethanol gave the *decahydro-compound benzoate* (1·1 g., 72%) as prisms, m. p. 137—139° (Found: C, 81·9; H, 8·2. $C_{22}H_{26}O_2$ requires C, 81·95; H, 8·1%). Hydrolysis gave an oily alcohol with no selective ultraviolet absorption.

Oxidation of this benzoate (100 mg.) in refluxing acetone (5 ml.) with potassium permanganate (100 mg.) gave the benzoate (II) (70 mg.) as needles, m. p. and mixed m. p. 160°.

trans-2β-*Benzoyloxy*-1 : 2 : 3 : 4 : 5 : 6 : 7 : 8 : 9 : 10 : 11 : 12-*dodecahydro*-12-*methylphenanthrene* (IV).—The benzoate (III) (200 mg.) in ethyl acetate (5 ml.) was shaken with hydrogen over palladised calcium carbonate. Filtration, evaporation, and crystallisation from ethanol gave the *dodecahydro-compound benzoate* (182 mg.) as plates, m. p. 118—121° (Found: C, 81·2; H, 8·5. $C_{22}H_{28}O_2$ requires C, 81·4; H, 8·7%). This was unaffected by permanganate in refluxing acetone.

Epoxidation of the Decahydro-compound Benzoate.—The benzoate (III) (200 mg.) was stirred in chloroform (6·0 ml.) with 90% formic acid (3·0 ml.) and 30% hydrogen peroxide (6·0 ml.) for 15 hr. Ether and water were added and the organic layer was washed and evaporated. The residue crystallised from ethanol, to give the *diepoxide* (V) (140 mg.) as prisms, m. p. 176—178° (Found: C, 74·8; H, 7·6. $C_{22}H_{26}O_4$ requires C, 74·55; H, 7·4%), having no infrared hydroxyl or ketone absorption.

Epoxidation of the Dodecahydro-compound Benzoate.—The benzoate (IV) (100 mg.) was epoxidised as above. Crystallisation from methanol gave the *monoepoxide* (VI) (70 mg.) as prisms, m. p. 120—122° (Found: C, 77·5; H, 8·25. $C_{22}H_{28}O_3$ requires C, 77·6; H, 8·3%).

Hydrogenation of the Dodecahydro-compound Benzoate.—The benzoate (IV) (100 mg.) in ether (5 ml.) and glacial acetic acid (5 ml.) was shaken with hydrogen over Adams catalyst. The product crystallised from ethanol to give the cyclo*hexanecarboxylate* (62 mg.) analogous to (IV), as prisms, m. p. 54—58° (Found: C, 80·35; H, 10·6. $C_{22}H_{34}O_2$ requires C, 79·95; H, 10·4%).

Ozonolysis of the Decahydro-compound Benzoate.—The benzoate (III) (200 mg.) in ethyl acetate (20 ml.) was ozonised at −60° until a permanent blue colour was obtained. The solvent was removed under reduced pressure, and the residue boiled with water (10 ml.) for 30 min. Ether-extraction gave an oil which crystallised from ethanol to give an unsaturated *ketone* (60 mg.) as prisms, m. p. 149—151° (Found: C, 78·8; H, 7·25. $C_{22}H_{24}O_3$ requires C, 78·5; H, 7·2%), $\nu_{max.}$ 1677 cm.$^{-1}$ in Nujol. The 2 : 4-*dinitrophenylhydrazone* formed dark red plates, m. p. 272—274°, from dioxan–ethanol (Found: C, 65·3; H, 5·4; N, 10·9. $C_{28}H_{28}O_6N_4$ requires C, 65·1; H, 5·5; N, 10·85%).

cis-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*Octahydro*-2β-*hydroxy*-12-*methylphenanthrene* (VIII).—2 : 3 : 4 : 9 : 10 : 12-Hexahydro-12-methyl-2-oxophenanthrene (5·0 g.) in ethanol (100 ml.) was shaken with hydrogen over Raney nickel. After uptake of 2 mol. of hydrogen the solution was filtered and evaporated. The residue was benzoylated, giving the *cis*-2α-benzoate (5·2 g.), m. p. 150—154° (from ethanol), of the alcohol (VII). Concentration of the mother-liquor and crystallisation from ethanol gave the cis-2β-*benzoate* (1·45 g.) as plates, m. p. 96° (Found: C, 82·15; H, 7·6. $C_{22}H_{24}O_2$ requires C, 82·5; H, 7·55%). Alkaline hydrolysis gave the free cis-2β-*alcohol* (VIII), forming prisms, m. p. 69—70°, from light petroleum (b. p. 60—80°) (Found: C, 83·75; H, 9·6. $C_{15}H_{20}O$ requires C, 83·3; H, 9·3%).

[1] Howell and Taylor, *J.*, 1958, 1248.
[2] Walker, *J.*, 1935, 1585; cf. Robinson, *J.*, 1936, 1089.

Oxidation of the alcohol (VIII) as described for the cis-2α-isomer [1] gave the known *cis*-ketone (semicarbazone, m. p. 196—198°).

cis-1 : 2 : 3 : 4 : 5 : 8 : 9 : 10 : 11 : 12-*Decahydro-2α-hydroxy-12-methylphenanthrene* (X).—The *cis*-2α-alcohol (VII) (1·5 g.) was reduced as described for the *trans*-series, with sodium (12 g.), methanol (100 ml.), and liquid ammonia (180 ml.). The *cis*-decahydro-2α-alcohol (1·2 g., 80%) formed needles, m. p. 87—89°, from light petroleum (b. p. 60—80°) (Found: C, 82·2; H, 10·2. $C_{15}H_{22}O$ requires C, 82·5; H, 10·2%). The ultra-violet absorption spectrum showed no characteristic maximum. The derived *benzoate* formed plates, m. p. 106—108°, from ethanol (Found: C, 82·0; H, 8·1. $C_{22}H_{26}O_2$ requires C, 81·95; H, 8·1%). Both the alcohol and the benzoate readily formed mixed crystals of sharp melting point with the parent aromatic compounds.

cis-2-α-*Benzoyloxy*-1 : 2 : 3 : 4 : 5 : 6 : 7 : 8 : 9 : 10 : 11 : 12-*dodecahydro*-12-*methylphenanthrene*.—The above *cis*-decahydro-2α-benzoate (100 mg.) in ethyl acetate (5 ml.) was shaken with hydrogen over palladised calcium carbonate. Filtration and evaporation gave a residue which on crystallisation from ethanol gave the *benzoate* (80 mg.) as plates, m. p. 111—113° (Found: C, 81·5; H, 9·0. $C_{22}H_{28}O_2$ requires C, 81·4; H, 8·7%), of compound (XI).

2 : 3 : 4 : 9 : 10 : 12-*Hexahydro*-6-*methoxy*-12-*methyl*-2-*oxophenanthrene* (XII).—7-Methoxy-1-methyl-2-tetralone (32 g.) was dissolved in a solution from sodium (4·0 g.) and methanol (100 ml.), and the whole added during 1 hr. to 4-chlorobutan-2-one (20 g.) in methanol (100 ml.) with stirring under nitrogen. After a further 30 min. a solution from sodium (4·0 g.) and methanol (100 ml.) was added during 15 min., and the mixture stirred for 45 min. at room temperature and then for 30 min. at the b. p. After addition of dilute sulphuric acid and ether, the ether layer was washed and evaporated, and the residue distilled. A pale yellow oil (31·9 g.), collected at 185°/0·3 mm., crystallised on dilution with ether and light petroleum (b. p. 40—60°) to give the pure tricyclic ketone (21·1 g.), m. p. 62°. Chromatography of the mother-liquor gave a further amount (2·6 g., total 58%).

trans-2β-*Benzoyloxy*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydro*-6-*methoxy*-12-*methylphenanthrene* (cf. XIII).—*trans*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-Octahydro-6-methoxy-12-methyl-2-oxophenanthrene [1] (100 mg.) in ethanol (10 ml.) was shaken with hydrogen over Adams catalyst. After filtration and evaporation the oily residue was benzoylated. The *benzoate* (110 mg.) formed colourless plates, m. p. 141—142°, from ethanol (Found: C, 78·5; H, 7·6. $C_{23}H_{26}O_3$ requires C, 78·8; H, 7·5%).

1 : 2 : 3 : 4 : 6 : 7 : 8 : 9 : 10 : 11α : 12 : 14β-*Dodecahydro*-2β-*hydroxy*-12-*methyl*-6-*oxophenanthrene* (XIV).—(*A*) *trans*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-Octahydro-2β-hydroxy-6-methoxy-12-methylphenanthrene (XIII) (2·5 g., from reduction of the ketone by lithium aluminium hydride) in ether (100 ml.) was added to liquid ammonia (300 ml.) containing lithium (0·5 g.). Methanol was added dropwise until the blue colour disappeared. More lithium (3 × 0·5 g.) was then added, and the colour discharged with methanol each time. After evaporation of the ammonia, ether and water were added, the ether layer was evaporated, and the residue refluxed for 3 hr. with ethanol (150 ml.), water (25 ml.), and concentrated hydrochloric acid (25 ml.). The oil isolated with ether was chromatographed on alumina (100 g.) in benzene. Benzene containing chloroform (10%) eluted an oil, crystallising from ether to give the *keto-alcohol* (0·5 g.) as yellow prisms, m. p. 118—120° (Found: C, 76·6; H, 10·0. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·5%), $\lambda_{max.}$ (in EtOH) 239 mμ (log ε 4·08), $\nu_{max.}$ (in Nujol) 1650, 3421 cm.$^{-1}$. The 2 : 4-*dinitrophenylhydrazone* formed red plates, m. p. 236—237° (decomp.), from dioxan–ethanol (Found: C, 60·9; H, 6·3; N, 13·3. $C_{21}H_{26}O_5N_4$ requires C, 60·85; H, 6·3; N, 13·5%). Crystallisation of this from acetic acid gave the *dinitrophenylhydrazone acetate* as dark red prisms, m. p. 239—241° (decomp.) (Found: C, 60·2; H, 6·1; N, 11·9. $C_{23}H_{28}O_6N_4$ requires C, 60·5; H, 6·2; N, 12·3%). The *ketone benzoate* formed plates, m. p. 174—175°, from methanol (Found: C, 78·0; H, 8·0. $C_{22}H_{26}O_3$ requires C, 78·1; H, 7·7%); acid-hydrolysis regenerates the alcohol, but alkali causes resinification.

(*B*) 2 : 3 : 4 : 9 : 10 : 12-Hexahydro-6-methoxy-12-methyl-2-oxophenanthrene (XII) (2·5 g.) was reduced with sodium (12 g.) and methanol (125 ml.) in liquid ammonia (200 ml.) as described for the preparation of compound (III). The product, after acid-hydrolysis as in method (*A*), was chromatographed on alumina (100 g.). Benzene and benzene containing chloroform (10%) eluted a non-ketonic oil, which after benzoylation crystallised from ethanol to give 2β-*benzoyloxy*-1 : 2 : 3 : 4 : x : x : x : x : 9 : 10 : 11 : 12-*dodecahydro*-12-*methylphenanthrene* (XVI) (345 mg.) as prisms, m. p. 113—116° (Found: C, 81·5; H, 9·0. $C_{22}H_{28}O_2$ requires C, 81·5; H, 8·7%). Benzene containing chloroform (20%) gave first the isomeric 14α-keto-alcohol (XV), isolated as

its *benzoate* (140 mg.); this crystallised from methanol in prisms, m. p. 174—175°, giving a strong depression with its isomer (Found: C, 78·1; H, 7·9. $C_{22}H_{26}O_3$ requires C, 78·1; H, 7·7%), $\lambda_{max.}$ (in EtOH) 241 mμ (log ε 3·87), $\nu_{max.}$ (in Nujol) 1667 cm.$^{-1}$. The infrared spectrum was very similar to that of the isomer. Further elution with benzene containing chloroform (20%) gave the 14β-keto-alcohol (410 mg.), crystallising from ether in yellow prisms, m. p. 118—120°, identical with the previous sample. Benzoylation of the mother-liquors gave the 14β-keto-benzoate (35 mg.), m. p. and mixed m. p. 174—175°.

Hydrogenation of the Dodecahydro-compound Benzoate (cf. XVI).—Hydrogenation over Adams catalyst in acetic acid gave the completely hydrogenated 2β-cyclo*hexanecarbonyloxyperhydro*-12-*methylphenanthrene* which crystallised from ethanol in plates, m. p. 66—68° (Found: C, 79·0; H, 10·95. $C_{22}H_{36}O_2$ requires C, 79·5; H, 10·9%).

Hydrogenation of the 14β-*Keto-alcohol* (XVI).—This keto-alcohol (250 mg.) in ethanol (10 ml.) was shaken with hydrogen over palladised calcium carbonate. The solution was filtered and evaporated, the residue crystallised from ether to give the *saturated keto-alcohol* (XVII) (100 mg.) as prisms, m. p. 98—102° (Found: C, 76·5; H, 10·0. $C_{15}H_{24}O_2$ requires C, 76·2; H, 10·1%). The *dinitrophenylhydrazone* was an amorphous orange solid, m. p. 180—220° (Found: C, 60·5; H, 6·6; N, 13·0. $C_{21}H_{28}O_5N_4$ requires C, 60·6; H, 6·8; N, 13·45%). The *benzoate* formed prisms, m. p. 175—177°, from methanol (Found: C, 77·7; H, 8·6. $C_{22}H_{28}O_3$ requires C, 77·6; H, 8·3%).

trans-anti-trans-7-*Furfurylideneperhydro*-2-*hydroxy*-6-*oxophenanthrene* (XVIII).—The ketone (XVII) (120 mg.) in methanol (3·0 ml.) was kept overnight under nitrogen with 33% sodium hydroxide solution (2·0 ml.) and furfuraldehyde (100 mg.). Ether and water were added, and the organic layer was washed neutral and evaporated. The residue crystallised from methanol to give the *furfurylidene-ketone* (80 mg.) as yellow prisms, m. p. 197—207° (Found: C, 76·1; H, 8·3. $C_{20}H_{26}O_3$ requires C, 76·4; H, 8·3%), $\nu_{max.}$ (in Nujol) 1673 cm.$^{-1}$.

6β-*Acetoxy*-1β : 2α-*di*(*methoxycarbonylmethyl*)-9β-*methyl*-trans-*decalin* (XIX).—The above furfurylidene derivative (140 mg.) was acetylated and then ozonised at −80° in ethyl acetate (20 ml.) until a strong blue colour persisted. The solvent was evaporated under reduced pressure, and acetic acid (10 ml.), water (2·5 ml.) and 30% hydrogen peroxide (1·0 ml.) were added. After being kept overnight the whole was extracted with ether, and the extract washed and evaporated. The residue was esterified with diazomethane, and then crystallised from methanol to give the *acetate dimethyl ester* (129 mg.) as prisms, m. p. 103° (Found: C, 64·5; H, 8·7. $C_{19}H_{30}O_6$ requires C, 64·4; H, 8·5%). The *benzoate diacid* crystallised from methanol in prisms, m. p. 277° (Found: C, 66·9, 67·0; H, 7·5, 7·4; O, 25·0. $C_{22}H_{28}O_6$ requires C, 68·0; H, 7·3; O, 24·7%).

cis-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*Octahydro*-2α-*hydroxy*-6-*methoxy*-12-*methylphenanthrene* (XX).—2 : 3 : 4 : 9 : 10 : 12-Hexahydro-6-methoxy-12-methyl-2-oxophenanthrene (XII) (300 mg.) in ethanol (10 ml.) was shaken with hydrogen over Raney nickel. After filtration and evaporation the residue was benzoylated. Crystallisation from ethanol gave the cis-2α-*benzoate* (260 mg.) as prisms, m. p. 117—119° (Found: C, 78·7; H, 7·8. $C_{23}H_{28}O_3$ requires C, 78·8; H, 7·5%). Alkaline hydrolysis gave the free *alcohol*, crystallising from light petroleum (b. p. 60—80°) in needles, m. p. 98—100° (Found: C, 77·9; H, 9·3. $C_{16}H_{22}O_2$ requires C, 78·0; H, 9·0%).

cis-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*Octahydro*-6-*methoxy*-12-*methyl*-2-*oxophenanthrene* (XXI).—The *cis*-alcohol (200 mg.) in acetone (5 ml.) was oxidised by the procedure of Bowers *et al.*[3] Crystallisation from light petroleum (b. p. 60—80°) gave the cis-*ketone* (187 mg.) as prisms, m. p. 79—81° (Found: C, 78·3; H, 8·0. $C_{16}H_{20}O_2$ requires C, 78·65; H, 8·25%).

cis-2α-*Benzoyloxy*-1 : 2 : 3 : 4 : 6 : 7 : 8 : 9 : 10 : 11 : 12 : 14-*dodecahydro*-12-*methyl*-6-*oxophenanthrene* (cf. XXII).—The above *cis*-2α-alcohol (2·0 g.) was reduced with sodium (10 g.) in methanol (100 ml.) and liquid ammonia (180 ml.) as described above. After hydrolysis the crude product was chromatographed on alumina (100 g.). Benzene containing chloroform (20%) eluted an oil which after benzoylation crystallised from methanol, to give a 2-α-*benzoyloxydodecahydro*-12-*methylphenanthrene* (XXIII) (390 mg.) as plates, m. p. 102—104° (Found: C, 81·6; H, 8·8. $C_{32}H_{28}O_2$ requires C, 81·4; H, 8·7%). Further elution with the same mixture gave an impure isomer (170 mg.), crystallising from methanol in plates, m. p. 108—112° (Found: C, 81·5; H, 8·4%). Elution with benzene containing more chloroform (50%) gave an oil which after benzoylation crystallised from methanol to give the *keto-benzoate* (cf. XXII) (200 mg.) as

[3] Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2548.

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prisms, m. p. 124—126° (Found: C, 77·8; H, 8·1. $C_{22}H_{26}O_3$ requires C, 78·1; H, 7·7%), $\lambda_{max.}$ (in EtOH) 240 mμ (log ε 4·17), $\nu_{max.}$ (in Nujol) 1667 cm.$^{-1}$.

1 : 2 : 3 : 4 : 5 : 6 : 7 : 9 : 10 : 11α : 12 : 13α-*Dodecahydro*-2β-*hydroxy*-12-*methyl*-7-*oxophenanthrene* (XXV).—2 : 3 : 4 : 9 : 10 : 12-Hexahydro-7-methoxy-12-methyl-2-oxophenanthrene (XXIV) (1·0 g.) was reduced with sodium (5 g.) in methanol (50 ml.) and liquid ammonia (90 ml.) as usual. After acid-hydrolysis, the product was chromatographed on alumina (50 g.). Elution with benzene containing chloroform (5—20%) gave a middle fraction that crystallised from ether, to give the *keto-alcohol* (32 mg.) as yellow prisms, m. p. 122—124° [Found: C, 76·9; H, 9·3. $C_{15}H_{22}O_3$ requires C, 76·9; H, 9·5%), $\lambda_{max.}$ (in EtOH) 241 mμ (log ε 3·59)]. Benzoylation of material from the mother-liquors and crystallisation from methanol gave the *benzoate* of the same alcohol (133 mg.) as needles, m. p. 175° (Found: C, 77·7; H, 7·95. $C_{22}H_{26}O_3$ requires C, 78·1; H, 7·7%). Benzoylation of the crystalline alcohol gave the same substance.

Reduction of 2 : 3 : 4 : 9 : 10 : 12-*Hexahydro*-6 : 7-*dimethoxy*-2-*oxophenanthrene* (XXVI).—This ketone (2·05 g.) was reduced with sodium (15 g.) in methanol (100 ml.) and liquid ammonia (180 ml.). After acid-hydrolysis the product was chromatographed on alumina (100 g.). Benzene containing chloroform (50%) eluted an oil which on benzoylation gave the keto-benzoate (cf. XIV) (150 mg.), crystallising from methanol in plates, m. p. 174—175° undepressed with the previous specimen, and having an identical infrared spectrum.

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NOTES.

309. *Cyclisation and Debenzylation of* m-*Benzyloxyphenylpropionic Acid as Competitive Reactions.*

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DURING an investigation into ring-closures yielding 5-alkyloxyindan-1-ones attempts were made to cyclise *m*-benzyloxyphenylpropionic acid by Friedel–Crafts methods. Aluminium chloride invariably caused debenzylation but significant amounts (10—15%) of 5-benzyloxyindan-1-one survived when stannic chloride dissolved in benzene was used and the main product, 5-hydroxyindan-1-one, was relatively pure and in good yield (40—50%). The 5-benzyloxyindan-1-one was identical with a sample prepared by direct benzylation of 5-hydroxyindan-1-one. The partial retention of the benzyloxy-group and the clean debenzylation were considered to warrant the use of this system to study cyclisation and debenzylation as competitive reactions.

The reactions were followed by quantitative analysis of the products, the experiments being designed to test variables such as concentration of reactants, excess of reagents, time, temperature, and solvent composition. Separation of the product into acidic, phenolic ketonic, phenolic non-ketonic, neutral ketonic, neutral non-ketonic, and ether-insoluble polymeric fractions revealed considerable complexity. The neutral fraction contained, in addition to the required ketone, traces of higher-melting ketones, diphenylmethane, and occasionally benzyl chloride. The phenolic ketone, mainly 5-hydroxyindan-1-one, contained other ketones, one of which was probably a benzyl-substituted hydroxyindan-1-one $C_{16}H_{14}O_2$. Traces of 7-hydroxyindan-1-one derivatives were also detected. A violet complex always separated during the reaction and since a similar complex was precipitated during the cyclisation of the 5-methoxy-analogue (which was not however demethylated), the violet compound was presumed to be a ketone–catalyst complex and not an ether–catalyst compound. Retention of the benzyl group was associated with the use of a large excess of stannic chloride and the rapid separation of the violet complex, though a connection between the two could not be proved. The use of less than 1·5 mol. of stannic chloride resulted in a substantial recovery of acid, even at high temperatures. The course of the

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reaction was influenced by changes in scale and apparatus. Both cyclisation and debenzylation were inhibited at 0°, for 30% of the product was acidic after 18 hr. (with 2·3 mol. of catalyst) and, of the remainder, the phenolic fraction constituted 15% (w/w) instead of the 35—50% obtained between 5° and 15°.

The lag between mixing of the reactants (both dissolved in benzene) and separation of the complex varied between a few seconds and some minutes but no consistent temperature–time or concentration–time pattern was discernible. Since rapid elimination of the ketone–reagent complex favours retention of structure, the solubility of the complex is of prime concern and an attempt was made to vary the solubility by using mixtures of light petroleum, benzene, and chloroform as solvents.

The use of a large proportion of chloroform reduced precipitation and greatly increased the ratio of phenolic to neutral product (2 : 1), indicating increased debenzylation. The reverse effect could not be demonstrated because, unless the chloroform or benzene predominated, side-reactions became serious and the product complex and difficult to separate. The proportion of polymer was much higher in light petroleum and chloroform at 5° than in benzene. However, in benzene diphenylmethane was formed and constituted up to 35% of the neutral fraction. The alternative formation of diarylmethanes in the presence of, and polymers in the absence of, aromatic hydrocarbons has also been noted by Praill [1] in work on benzyl derivatives.

Other cyclising agents were tried under conditions milder than those normally employed; these included phosphorus oxychloride,[2,3] phosphoric oxide,[4,5] polyphosphoric acid,[6] anhydrous hydrofluoric acid,[7] and fluorosulphuric acid.[8] All gave viscous, non-ketonic products except the last, which in dilute chloroform solution at 0° gave small yields of very pure 5-benzyloxy- and 5-hydroxy-indan-1-one. The main reaction was evidently sulphonation, since most of the product was water-soluble.

Experimental.—m-*Benzyloxyphenylpropionic acid.* *m*-Hydroxyphenylpropionic acid [9] (30 g.) and pyridine (2 drops) were dissolved in a solution of sodium ethoxide [from sodium (9 g.)] in ethanol (200 ml.). Benzyl chloride (22·5 ml.) was added to the boiling solution which, refluxed for 1 hr., evaporated, diluted with water, washed with ether, chilled, and acidified, yielded m-*benzyloxyphenylpropionic acid* (36 g., 78%) in platelets, m. p. 86° (from dilute ethanol or acetic acid), b. p. 170°/0·05 mm. (Found: C, 75·2; H, 6·3%; titration equiv., 259. $C_{16}H_{16}O_3$ requires C, 75·0; H, 6·3%, equiv., 256). A portion was debenzylated with hydrobromic acid in acetic acid, yielding *m*-hydroxyphenylpropionic acid, m. p. 111—112°, not depressed on admixture with starting material.

5-*Benzyloxyindan*-1-*one.* (*a*) 5-Hydroxyindan-1-one [7] (1 g.) was refluxed with a solution of sodium ethoxide [from sodium (0·155 g.)] in ethanol (15 ml.) until it dissolved, and treated with freshly-redistilled benzyl chloride (0·86 g.) in ethanol (10 ml.). The mixture was refluxed for 1½ hr. and evaporated. Water was added, and the product extracted with ether, yielding 5-*benzyloxyindan*-1-*one* (0·93 g., 58%) as pale yellow prisms, m. p. 105·5—106° (from methanol) (Found: C, 81·1; H, 5·7. $C_{16}H_{14}O_2$ requires C, 80·7; H, 5·9%). The semicarbazone had m. p. 231° (from ethanol).

(*b*) *Cyclisation with stannic chloride.* *m*-Benzyloxyphenylpropionic acid (2·5 g.) in ether (12 ml.) was refluxed for 3 hr. with thionyl chloride (4 ml.) containing a trace of pyridine. After evaporation twice with benzene and ether, the acid chloride was substantially pure (Found: Cl, 12·7%; equiv., 140·2. $C_{16}H_{15}O_2Cl$ requires Cl, 12·9%; equiv., 137·4). It decomposed at 195°/0·25 mm.

The acid chloride from 2·5 g. of *m*-benzyloxyphenylpropionic acid in benzene (12 ml.) was

[1] Praill, *J.*, 1957, 3162.
[2] Freeman and Amstutz, *J. Amer. Chem. Soc.*, 1950, **72**, 1526.
[3] Albert and Linnell, *J.*, 1936, 88.
[4] Perkin and Robinson, *J.*, 1907, **91**, 1073, 1080, 1094.
[5] Birch and Smith, *J.*, 1951, 1885.
[6] Horning and Parker, *J. Amer. Chem. Soc.*, 1952, **74**, 3870.
[7] Johnson, Anderson, and Shelberg, *ibid.*, 1944, **66**, 218.
[8] Baker, Coates, and Glockling, *J.*, 1951, 1376.
[9] Donbrow and Linnell, *J. Pharm. Pharmacol.*, 1952, **4**, 118.

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treated with freshly-redistilled stannic chloride (2·5 ml.) in benzene (7·5 ml.) at 2—4°. A violet sludge was deposited. After 15 min. this was decomposed with crushed ice, hydrochloric acid, and ether. The ether–benzene layer was filtered, washed with 5% sodium hydrogen carbonate solution, dilute sodium hydroxide solution, and water and evaporated, yielding a brown, mobile liquid (1·4 g.) from which 5-benzyloxyindan-1-one (0·2 g.) crystallised at 0°, a second crop (0·2 g.) being obtained after removal of diphenylmethane from the residue by distillation or crystallisation. It formed pale yellow prisms, m. p. 105·5—106° (from methanol or ethanol), not depressed on admixture with a sample obtained by benzylation (Found: C, 81·0; H, 5·9%). Its *semicarbazone* had m. p. 231° (from ethanol), not depressed on admixture with a sample from benzylation (Found: C, 69·8; H, 5·9; N, 14·1. $C_{17}H_{17}O_2N_3$ requires C, 69·2; H, 5·8; N, 14·2%).

From the aqueous alkaline extracts, 0·7 g. of an impure phenol, obtained on acidification and extraction with ether, yielded large crystals of 5-hydroxyindan-1-one,[7,10,11] m. p. 185° (from methanol). Its semicarbazone had m. p. 223°.

Cyclisations.—These were carried out on the 2·5 g. scale, conditions being varied as described in the Introduction. Some larger-scale runs (10 and 15 g.) were carried out. The acid chloride was freshly prepared in large batches, evaporated twice with solvent, and analysed before use.

The fractions were separated into acidic, phenolic, and neutral components and insoluble polymer. The uncrystallisable residues were checked for ketones and separated by use of Girard's reagent P into ketonic and non-ketonic fractions. Tests applied were (1) colour reaction with alcoholic ferric chloride (for 7-hydroxyindan-1-ones),[10] (2) reaction with hydriodic acid (for odour of benzyl iodide), (3) oxidation with chromic acid and reaction of products with Brady's reagent (for benzyl derivatives of non-ketonic fractions).[12,13] Traces of unidentified ketones were obtained together with a *benzyloxyindan-1-one* (?), pale yellow prisms, m. p. 220—224° (from ethanol), insoluble in water, soluble in sodium hydroxide solution; no colour with ferric chloride solution (Found: C, 80·3; H, 5·98%), 2 : 4-dinitrophenylhydrazone, m. p. 236—242° (decomp.) (from glacial acetic acid), 235—241° decomp. (from ethyl acetate).

I thank Prof. W. H. Linnell for his interest and advice.

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CHELSEA SCHOOL OF PHARMACY, CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY,
LONDON, S.W.3. [*Received, September 29th*, 1958.]

[10] Ingold and Pigott, *J.*, 1923, 1469.
[11] Brand and Horn, *J. prakt. Chem.*, 1927, **115**, 351, 376.
[12] Burton and Praill, *J.*, 1951, 522.
[13] *Idem*, *J.*, 1953, 827.

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310. *A Quantitative Ullmann Reaction.*

By P. H. GORE and (the late) G. K. HUGHES.

THE formation of diphenyls in the Ullmann reaction [1] has been much studied. Recently, Carlin and Foltz [2] have reported yields of the diphenyls of 46% from 1-iodo-4- and of 79% from 1-iodo-6-methyl-2-nitrobenzene, using 1 equiv. of copper powder, and, in the latter case, sand as a diluent to moderate the reaction. Earlier, Wittig and Stichnoth [3] obtained a similar yield (81%) in the latter reaction by careful addition of the copper, without the use of diluent. For the preparation of 2 : 2′-dinitrodiphenyl from *o*-iodonitrobenzene, Davey and Latter [4] recorded a yield of 65%. We have found that commercial samples of copper powder give irreproducible yields in this reaction, and that freshly precipitated copper, obtained by a modification of Ritchie's method,[5] is the most effective.

[1] Fanta, *Chem. Rev.*, 1946, **38**, 139.
[2] Carlin and Foltz, *J. Amer. Chem. Soc.*, 1956, **78**, 1997.
[3] Wittig and Stichnoth, *Ber.*, 1935, **68**, 930.
[4] Davey and Latter, *J.*, 1948, 264.
[5] Ritchie, *J. Proc. Roy. Soc., N.S.W.*, 1945, **78**, 161.

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By the use of approx. 4 equiv. of copper, and of careful temperature control, yields of 95—97% of 2 : 2′-dinitrodiphenyl were reproducibly obtained.

Experimental.—Copper powder. Oxide-free zinc dust was added to an excess of slightly acidified aqueous copper sulphate, the temperature not being allowed to rise above 40°. The precipitated copper was collected, washed free from copper and acid, and twice with dry acetone, and dried at 100°.

2 : 2′-Dinitrodiphenyl. Copper powder (30 g.) was added in small portions, with occasional stirring, to *o*-iodonitrobenzene (30 g.) in a thick-walled conical flask kept at 190°. After 2½ hr. at 190°, heating was continued at 240° for 2½ hr. The product was extracted with hot benzene, the filtered extract on evaporation giving substantially pure 2 : 2′-dinitrodiphenyl (29·2 g., 96%; m. p. 122—124°, or 124° after one crystallisation from ethanol).

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311. 1- *and* 2-*Anthraldehydes.*

By P. H. GORE.

IN connection with other work, the syntheses of 1- and 2-anthraldehydes were investigated. Attempted preparation of 1-anthraldehyde by the Stephen reduction [1] of 1-anthronitrile proved abortive; this is in keeping with the observation [2] that in this reaction 1-naphthaldehyde is formed only to about 7% under conditions which give a 91% yield of 2-naphthaldehyde.

1- and 2-Anthronitriles were converted into the corresponding aldehydes by use of a deficiency of lithium aluminium hydride, a method which was successful in the preparation [3] of benzaldehyde and 2-naphthaldehyde in good yield. Addition of benzene was necessary to increase the solubility of the anthronitriles in ether, but more than 30% (by volume) precipitated the hydride and reduction did not take place. Even then, reduction was incomplete, and large amounts of the anthronitriles were recovered. The aldehydes were isolated as 2 : 4-dinitrophenylhydrazones, which were readily separable from nitriles. Regeneration was by use of pyruvic acid.[4]

Light absorption of some anthracene derivatives [a] (λ *in* Å).

	1-Anthryl				2-Anthryl			
Derivative	$\lambda_{max.}$	$\varepsilon_{max.}$	$\lambda_{max.}$	$\varepsilon_{max.}$	$\lambda_{max.}$	$\varepsilon_{max.}$	$\lambda_{max.}$	$\varepsilon_{max.}$
Chloro-	2500	93,800 [b]	3650	6,400	2555	153,000 [a]	3600	5,750
	2570	105,000	3840	5,750	3280	1,900	3800	4,900
	3480	4,050			3420	3,300		
Nitrile	2570	87,200	3780	6,050	2510	73,000 [c]	3580	4,100
	3580	4,500	3960	5,100	2570	103,000	3760	3,750
					2640	73,000	3920	2,600
					3430	3,000		
Aldehyde	2430	55,700	3680	3,700	2590	61,800	3430	4,300
	2640	51,600	3970	4,750	2650	61,800	3640	4,300
	2800	24,400			2700	57,800	3840	3,700
					2810	51,500	4050	2,800
					3280	2,800		
Aldehyde 2 : 4-dinitrophenylhydrazone			4300	23,200	3960	28,400		

[a] In chloroform, unless otherwise stated. [b] Inflection. [c] In ethanol

The analytical figures obtained for the 2-anthraldehyde are 1·5% low for carbon, possibly owing to contamination by 2-anthroic acid. There is little doubt as to its chemical

[1] Stephen, *J.*, 1925, **127**, 1874; cf. Leber, *J. Amer. Chem. Soc.*, 1949, **71**, 2862.
[2] Williams, *ibid.*, 1939, **61**, 2248.
[3] Braude and Gore, *J.*, in the press.
[4] Mattox and Kendall, *J. Amer. Chem. Soc.*, 1948, **70**, 882.

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identity, however, since it can be reconverted into its dinitrophenylhydrazone in high yield.

The starting materials were 1- and 2-chloroanthracene,[5] which were converted into the nitriles by cuprous cyanide in dry pyridine.[6-8] Overall yields were about 20% for the four stages from the chloroanthraquinones.

Light-absorption data are given in the Table; there were no unexpected features. The position of the *K*-band of the two dinitrophenylhydrazones [9] points to a greater conjugating power of the 1- than of the 2-anthryl position, as expected from theory.[10]

Experimental

The microanalyses were by Mr. F. H. Oliver and his staff and the light-absorption measurements by Mrs. I. Boston, of the Department of Chemistry, Imperial College.

1-*Chloroanthracene.*—The method of Fischer and Ziegler [5] was used. The yield was increased to 92% by heating the mixture for 3 hr. instead of 0·5 hr. The product formed yellow crystals, m. p. 81° (quoted [5] m. p. 79°).

1-*Anthronitrile.*—1-Chloroanthracene (16 g.) and cuprous cyanide (8·2 g.) were heated with pyridine (16 ml.) (freshly distilled from potassium hydroxide) at 245—255° (bath temp.) for 24 hr. During the last hour the pyridine was allowed to distil off. After cooling, the dark residue was repeatedly extracted with hot alcohol, the extracts were evaporated to dryness, and the residue chromatographed from benzene on alumina. The eluate yielded nearly pure 1-anthronitrile (13·5 g., 89%), m. p. 137—138°, which on recrystallisation afforded yellow plates, m. p. 139—140° (Found: C, 89·0; H, 4·7; N, 6·5. Calc. for $C_{15}H_9N$: C, 88·6; H, 4·5; N, 6·9%) (Dieuel [11] quotes m. p. 126°).

1-*Anthraldehyde* 2 : 4-*Dinitrophenylhydrazone.*—1-Anthronitrile (10 g.) was dissolved in ether (350 ml.)–benzene (150 ml.), and to the stirred solution at 0°, lithium aluminium hydride (1·05 g.) in ether (100 ml.) was added during 5 min. After being stirred and heated under reflux for 1 hr., the mixture was set aside for 12 hr. It was then again cooled to 0°, and excess of 2N-sulphuric acid was carefully added. The organic layer was separated, washed, and evaporated. The residual solid, in hot alcohol, was treated with a large excess of ethanolic 2 : 4-dinitrophenylhydrazine sulphate. Extraction of the red precipitate (9·5 g.) with boiling methanol (300 ml.), filtration whilst hot, and cooling gave 1-anthronitrile (5·4 g.; m. p. 138—140°) and left undissolved 1-*anthraldehyde* 2 : 4-*dinitrophenylhydrazone* (3·2 g., 37% after allowance for recovered anthronitrile), m. p. 279—281°. Crystallisation from pyridine gave bright red plates, m. p. 282—283° (Found: C, 65·1; H, 4·2; N, 14·4. $C_{21}H_{14}O_4N_4$ requires C, 65·3; H, 3·7; N, 14·5%).

1-*Anthraldehyde.*—The 2 : 4-dinitrophenylhydrazone (4·0 g.) was suspended in chloroform (75 ml.); 90% pyruvic acid (8 ml.) and acetic acid saturated with hydrogen bromide (5 ml.) were added, and the mixture was gently boiled for 17 hr. The mixture was cooled, and extracted with water, aqueous sodium hydrogen carbonate, and again with water, dried (Na_2SO_4), and evaporated. Chromatography from benzene on alumina, followed by crystallisation from acetone, and finally from carbon tetrachloride, gave large dark red prisms of 1-*anthraldehyde* (1·35 g., 64%; m. p. 126·5—127·5°) (Found: C, 87·0; H, 5·1. $C_{15}H_{10}O$ requires C, 87·4; H, 4·9%). There was no reaction with sodium hydrogen sulphite.

2-*Chloroanthracene.*—Prepared by the method of Fischer and Ziegler,[5] but with 6 hours' heating, the 2 chloro-compound was obtained in 83% yield. Purified by chromatography on alumina and recrystallisation from acetic acid the product had m. p. 217—218° (quoted [5] m. p. 215°). In benzene solution, it exhibits an intense violet fluorescence.

2-*Anthronitrile.*—This was prepared as described for the 1-isomer and obtained in 81% yield. After recrystallisation from acetic acid it had m. p. 200° (quoted [12] m. p. 200°).

2-*Anthraldehyde.*—The method used was identical with that described for the 1-isomer. The

[5] Fischer and Ziegler, *J. prakt. Chem.*, 1912, **2**, **86**, 293.
[6] Cf. Beyer and Fritsch, *Ber.*, 1941, **74**, 494.
[7] Newman, *J. Amer. Chem. Soc.*, 1937, **59**, 2472.
[8] Schultz, Goldberg, Ordas, and Carsch, *J. Org. Chem.*, 1940, **11**, 307.
[9] Braude and Jones, *J.*, 1945, 498.
[10] Coulson and Longuet-Higgins, *Proc. Roy. Soc.*, 1947, *A*, **192**, 16.
[11] Dieuel, *Ber.*, 1906, **39**, 926.
[12] Waldmann and Oblath, *Ber.*, 1938, **71**, 366.

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2 : 4-*dinitrophenylhydrazone* (31%, based on nitrile consumed) formed deep orange tufts (from pyridine–ethanol), m. p. 297—298° (Found: C, 65·6; H, 4·1; N, 14·9%). 2-*Anthraldehyde* (82%) had m. p. 203—204° after recrystallisation from acetone–ethanol) (Found: C, 85·8, 85·9; H, 4·9, 5·0%).

This work was begun during the tenure of a C.S.I.R.O. studentship (P. H. G.). I thank Imperial Chemical Industries Limited, Dyestuffs Division, and Dr. R. S. Barnes, for generous gifts of 1- and 2-chloroanthraquinone, and acknowledge advice from (the late) Professor E. A. Braude.

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London, W.3. [*Received, November 4th*, 1958.]

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312. *The Dielectric Constant of Ethyl Chloride.*

By W. R. Longworth and P. H. Plesch.

The dielectric constant of liquid ethyl chloride has not been reported. As we required this in connection with other work, we measured it with Bender's apparatus,[1] using a closed cell with concentric cylindrical electrodes. It was calibrated with carbon tetrachloride (17·6°), chloroform (17·2°), methylene dichloride (0° and 17·2°), and ethylene dichloride (16·9°), by using the known dielectric constants of these substances at the given temperatures.[2] The ethyl chloride was a commercial product, f. p. $-136{\cdot}0° \pm 0{\cdot}2°$ (lit.,[3] f. p. −136·4°), having a completely flat freezing curve. Temperatures were measured with a pentane thermometer, which was calibrated by the freezing points of water and of specially purified specimens of carbon tetrachloride (−23·0°) and methylene dichloride (−96·7°).

The results (Table) can be represented by the equation

$$\varepsilon_{t'} = \varepsilon_t - 5{\cdot}93 \times 10^{-2}(t' - t)$$

where ε_t and $\varepsilon_{t'}$ are the dielectric constants at temperatures t and t'. The interpolated value of ε at 0° being used, this can be written for convenient use in the form

$$\varepsilon_t = 12{\cdot}25 - 5{\cdot}93 \times 10^{-2}t$$

where t is in ° c. We estimate the uncertainty in the dielectric constant values to be less than ±2%.

Temp.		−72°	−65°	−47°	−34°	−32°	−22°	−12°	−2°
Dielectric constant	Run 1	—	—	15·05	14·30	—	13·55	12·95	12·50
	Run 2	—	—	15·15	—	14·30	13·55	12·95	12·50
	Run 3	16·50	16·10	15·05	—	14·30	13·55	12·80	12·35

We acknowledge grants from Esso Research Limited (to W. R. L.).

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Keele, Staffordshire. [*Received, November 11th*, 1958.]

[1] Bender, *J. Chem. Educ.*, 1946, **23**, 179.
[2] National Bureau of Standards, Circular 514.
[3] Timmermans, "Physico-Chemical Constants of Pure Organic Liquids," Elsevier Publ. Co. Inc., New York, 1950.

313. *Characterisation of Aromatic Amines by* p-p'-*Nitrophenylazobenzoyl Derivatives.*

By El S. Amin.

p-p'-Nitrophenylazobenzoyl chloride, already used for identification and separation of alcohols [1] and aliphatic amines,[2] has now been similarly applied to aromatic amines. The chloride has given acyl derivatives in fairly good yields on reaction with nine aromatic amines in pyridine–benzene at convenient temperatures. The acyl derivatives melt sharply and at much higher temperatures (in a convenient range) than do other derivatives.[3,4] Moreover, the m. p.s differ sufficiently to be useful criteria. *o*-Aminophenol reacted with the reagent to produce both *N*- and *O*-acyl compounds whereas *p*-phenylazobenzoyl chloride does not.[3] Occasionally contaminating nitrophenylazobenzoic acid has to be removed chromatographically. The acyl derivatives are bright red, an advantage in chromatography.

Experimental.—Evaporations were under reduced pressure at 50°. M. p.s were determined on a Kofler microscope stage.

Preparation of acyl derivatives. The aromatic amine (0·5 mmole) and *p-p'*-nitrophenylazobenzoyl chloride [1] (0·725 mmole) were refluxed in 1 : 1 pyridine–benzene (100 ml.) for 6 hr. The mixture was treated with water and extracted with 1 : 1 benzene–ether (250 ml.). The extract was washed with 20% sulphuric acid, filtered, washed with water, aqueous sodium carbonate, and water, concentrated to *ca.* 50 ml., and filtered through activated alumina. The main, lower red band was eluted with benzene, and the product recrystallised from acetone (as needles). The *p-p'*-nitrophenylazobenzoyl derivatives shown in the Table were thus prepared

Acyl derivatives, $NO_2 \cdot C_6H_4 \cdot N_2 \cdot C_6H_4 \cdot CO \cdot NHR$.

			Found (%)				Required (%)		
Aromatic amine	Colour of deriv.	M. p.	C	H	N	Formula	C	H	N
Aniline	Orange	270°	65·8	4·2	16·4	$C_{19}H_{14}O_3N_4$	65·9	4·1	16·2
o-Anisidine	Orange-red	228	—	—	14·9	$C_{20}H_{16}O_4N_4$	—	—	14·9
β-Naphthylamine	Orange	270	—	—	13·9	$C_{23}H_{16}O_3N_4$	—	—	14·1
α-Naphthylamine	Orange	263	69·8	4·1	13·7	$C_{23}H_{16}O_3N_4$	69·7	4·1	14·1
o-Toluidine	Orange	224	66·9	4·5	—	$C_{20}H_{16}O_3N_4$	66·7	4·5	—
m-Toluidine	Orange	208	66·8	4·6	—	$C_{20}H_{16}O_3N_4$	66·7	4·5	—
p-Toluidine	Orange	308	66·5	4·4	—	$C_{20}H_{16}O_3N_4$	66·7	4·5	—
o-Phenylenediamine	Red	306	62·1	3·7	18·0	$C_{32}H_{22}O_6N_8$	62·5	3·6	18·2
o-Aminophenol	Red	240	62·3	3·9	—	$C_{32}H_{21}O_7N_7$	62·4	3·4	—

in 90—95% yield. The first seven were recrystallised from acetone, and the last two from dimethylformamide.

Hydrolysis by potassium hydroxide (1 mole) in 2-methoxyethanol for a few hours at 50° regenerated the aromatic amine.

Chromatography. The two layers formed by a 5 : 1 (v/v) mixture of 65% aqueous dimethylformamide and carbon tetrachloride were separated. A tube (*ca.* 40 cm. long, 2 cm. diam.) was half filled with the dimethylformamide layer. A 1 : 1 (w/w) mixture (20 g.) of the other layer and kiesulguhr impregnated with dimethyloxosilane [2] was made into a sludge with the carbon tetrachloride layer (40 c.c.) and added to the column. When the column had drained, the acyl derivatives (2 mg.), dissolved in the carbon tetrachloride layer, were added and the chromatogram was developed with the dimethylformamide layer under slight suction. Elution can be hastened with 75% dimethylformamide.

Nearly a complete separation was achieved of the derivatives of (i) aniline and *o*-anisidine; (ii) *o*-aminophenol and *o*-phenylenediamine; (iii) di-*n*-butylamine and α-naphthylamine; (iv) *o*-, *m*-, and *p*-toluidine.

Alexandria University, Egypt. [*Received, November 11th*, 1958.]

[1] Hecker, *Chem. Ber.*, 1955, **88**, 1666; Amin and Hecker, *ibid.*, 1956, **89**, 695.
[2] Amin, *J.*, 1957, 3764.
[3] Woolfolk and Riberts, *J. Org. Chem.*, 1956, **21**, 436.
[4] McElvain, "The Characterisation of Organic Compounds," Macmillan, New York, 1946.

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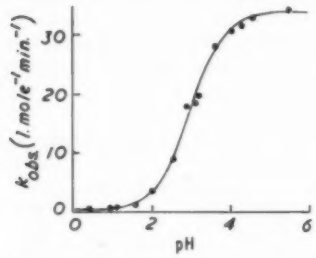
314. *Catalysis by Lead Ion of the Formation of Ethylenediaminetetra-acetatocobalt(III) from the Corresponding Monobromo-complexes.*

By W. C. E. Higginson and M. P. Hill.

Identical first-order rate constants, $k = -\mathrm{d} \ln [(\mathrm{H})\mathrm{CoYBr}]/\mathrm{d}t$, have been found [1] for the formation in aqueous solution of the sexidentate complex ion ethylenediaminetetra-acetatocobalt(III), CoY^-, by elimination of the ligand Br^- from the corresponding quinquedentate complexes, CoYBr^{2-} and HCoYBr^-. (The value of the rate constant quoted in ref. 1 is erroneous and should read 4×10^{-4} min.$^{-1}$.) The unbound carboxylate group present in CoYBr^{2-}, and the carboxylic acid group present in the conjugate acid, HCoYBr^-, evidently take no part in the rate-determining step in these reactions.

The formation of CoY^- from these complexes is strongly catalysed by Ag^+ and Hg^{2+}.[2] Lately it has been reported [3] that Cd^{2+}, Zn^{2+}, and Fe^{3+} are effective catalysts, although less so than Ag^+ and Hg^{2+}. These observations are confirmed by our recent experiments; we also find that Tl^{3+} is very effective.

In a more detailed investigation of the kinetics of reaction between excess of Pb^{2+} and these bromo-complexes in aqueous perchlorate solutions, we find a variation in the second-order rate constant, $k_{obs.} = -[\mathrm{Pb}^{2+}]^{-1}\mathrm{d} \ln [\text{bromo-complex}]_{total}/\mathrm{d}t$, with pH similar to that observed in the uncatalysed elimination of $\mathrm{H_2O}$ from the quinquedentate aquo-complexes, $\mathrm{CoYH_2O}^-$ and $\mathrm{HCoYH_2O}$.[1] Similarly, we interpret the results shown in the Figure in terms of rate constants for the reaction of CoYBr^{2-} and HCoYBr^- with Pb^{2+}, and the acid dissociation constant, K, for HCoYBr^-. At 25° and ionic strength 1·0, the second-order constants, $k_1 = -[\mathrm{Pb}^{2+}]^{-1}\mathrm{d} \ln[\mathrm{CoYBr}^{2-}]/\mathrm{d}t$ and $k_2 = -[\mathrm{Pb}^{2+}]^{-1}\mathrm{d} \ln [\mathrm{HCoYBr}^-]/\mathrm{d}t$, are 33·8 ± 0·3 and 0·15 ± 0·02 l. mole^{-1} min.$^{-1}$, respectively, and $pK = 2{\cdot}96 \pm 0{\cdot}03$. The theoretical line constructed from these values is shown in the Figure. In obtaining k_2 it was necessary to make a small correction for the uncatalysed reaction, the rate constant of which is *ca.* 10^{-3} min.$^{-1}$ under these conditions.



The first-order rate constant for the elimination of $\mathrm{H_2O}$ from $\mathrm{CoYH_2O}^-$ is greater than that for the corresponding reaction of $\mathrm{HCoYH_2O}$. This has been ascribed to an intramolecular S_N2-type reaction in the former complex, the unbound carboxylate group displacing the ligand $\mathrm{H_2O}$.[1] The carboxylic acid group in $\mathrm{HCoYH_2O}$ is considered to take no part in the rate-determining reaction of this complex; in this case the mechanism is of the type S_N1. We believe that electrostatic repulsion between the incipiently-formed Br^- and the unbound carboxylate group present in CoYBr^{2-} is responsible for the lack of participation of this group in the rate-determining step of the uncatalysed elimination reaction. We suggest that this repulsion is overcome by the presence of Pb^{2+} in the transition complex of the catalysed reaction so that the unbound carboxylate group can participate. Hence the rate of the CoYBr^{2-}–Pb^{2+} reaction will be greater than that of the HCoYBr^-–Pb^{2+} reaction in which the carboxylic acid group will still be inactive, as in the uncatalysed elimination reactions of HCoYBr^- and $\mathrm{HCoYH_2O}$. The Br^- is probably removed as the ion-pair, PbBr^+. The ratio of the rate constants for the formation of CoY^- from a quinquedentate complex and its conjugate acid appears to depend on the charge of the group eliminated from the transition complex. In the uncatalysed reactions of (i) the bromo-complexes, (ii) the aquo-complexes, and in (iii) the Pb^{2+}-catalysed reactions of the bromo-complexes,

[1] Shimi and Higginson, *J.*, 1958, 260.
[2] Schwarzenbach, *Helv. Chim. Acta*, 1949, **32**, 839.
[3] Dwyer and Garvan, *J. Amer. Chem. Soc.*, 1958, **80**, 4480.

the species lost are (i) Br^-, (ii) H_2O, (iii) $PbBr^+$, and the corresponding ratios are (i) 1 : 1, (ii) 7 : 1, (iii) 200 : 1.

It is proposed to extend this work to include similar studies of the catalysis by other cations, in the hope of establishing a relation between their reactivity and their affinity for halide ions, and possibly also their ionic radii. As foreshadowed above, the effect of the charge of the catalyst cation is also likely to be of interest.

Experimental.—Potassium bromo(ethylenediaminetriacetatoacetic acid)cobalt(III) dihydrate was prepared and purified as previously described.[2] Other reagents were "AnalaR" or were purified by appropriate methods. Lead perchlorate was obtained in solution by dissolving freshly precipitated lead hydroxide in dilute perchloric acid. Sodium perchlorate solution was prepared by dissolving anhydrous sodium carbonate in 60% perchloric acid. Pyridinium perchlorate solution was obtained by dissolving redistilled pyridine in dilute perchloric acid.

Solutions for kinetic experiments were made by dissolving a known weight of the solid bromo-complex in dilute perchloric acid (pH 0·4—3) or pyridine–pyridinium perchlorate buffer mixtures (pH 3—5·5). The ionic strength was made 1·0 by the addition of sodium perchlorate solution. The pH of the solution was measured by meter at the beginning and end of each kinetic experiment. The meter was standardised against a 0·01M-perchloric acid solution containing 0·99M-sodium perchlorate; the pH of this solution was taken as 2·00. Initial concentrations of the bromo-complex were $0·5—2·0 \times 10^{-3}$M, and of Pb^{2+}, $0·5—8·0 \times 10^{-2}$M. The highest concentration of free pyridine was *ca.* 0·02M, present in the solutions of highest pH, and the highest concentration of pyridinium ion was 0·2M, in a solution of pH 3·1.

The reaction was followed spectrophotometrically (Unicam S.P. 500) by measurements at 535 mμ, the molecular extinction coefficients of CoY^- and $CoYBr^{2-}$ (or $HCoYBr^-$) at this wavelength being 337 and *ca.* 90, respectively. Other measurements at 574 mμ, at which wavelength the molecular extinction coefficients are identical (230), showed that the extent of side-reactions is small. Pb^{2+} being in considerable excess, plots of $\ln (D_\infty - D_t)$ against t were linear up to *ca.* 75% of reaction, D_∞ representing the optical density of the reaction solution in a given cell at the completion of reaction and D_t the optical density in the same cell at time t. Values of $k_{obs.}$ were obtained by dividing the negative gradients of these plots by the corresponding concentrations of Pb^{2+}. Experiments with different pyridine–pyridinium ion buffer concentrations, but similar pH values, showed that the rate of reaction was little affected by the concentration of the buffer. This buffer was used instead of the commoner acetate–acetic acid buffer in order to avoid the complication of complex formation between Pb^{2+} and acetate ions, the formation constant for $(PbCH_3{\cdot}CO_2)^+$ being *ca.* 100.[4]

The apparent pK of $HCoYBr^-$ was found to be $2·96 \pm 0·03$ at 25° and ionic strength 1·0 by pH titration, the meter being standardised as described above. The pH of this complex has previously been found to be $2·98 \pm 0·05$ at 20° and ionic strength 0·1.[5]

THE UNIVERSITY, MANCHESTER. [*Received, November 14th*, 1958.]

[4] Edmonds and Birnbaum, *ibid.*, 1940, **62**, 2367.
[5] Schwarzenbach and Heller, *Helv. Chim. Acta*, 1951, **34**, 576.

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315. *Electronic Structure, Chemical Reactivity, and Basicity of Purines and Pyrazolopyrimidines.*

By BERNARD PULLMAN.

MY collaborators and I have studied recently, by the molecular-orbital method, the electronic structure of fundamental natural purines [1,2] and of purine antimetabolites active in cancer chemotherapy.[3] A special study has been made of their basicity.[4] This research has been extended to pyrazolopyrimidines.[5] We now make some complementary

[1] Pullman, Pullman, and Berthier, *Compt. rend.*, 1956, **243**, 380.
[2] Pullman and Pullman, *Bull. Soc. chim. France*, 1958, 766.
[3] Pullman and Pullman, *Bull. Soc. chim. France*, 1958, 973.
[4] Nakajima and Pullman, *Bull. Soc. chim. France*, 1958, 1502.
[5] Pullman, Pullman, and Nakajima, *Bull. Soc. chim. France*, in the press.

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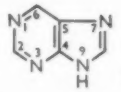
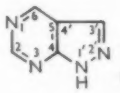
remarks in connection with Lynch, Robins, and Cheng's paper on ionisation constants of purines and pyrazolopyrimidines.[6] These authors, who then only had our first note on the structure of purines,[1] state that little reliance can be placed on the results of our calculations on the purine molecule because " the calculated charge densities at the various carbon atoms predict an incorrect order of reactivities towards nucleophilic reagents." This probably refers to the observation that $C_{(6)}$-substituents in purine are attacked by nucleophils preferentially to $C_{(2)}$-substituents, although our calculations indicated that $C_{(2)}$ is the more positive. However, the *relative* charge distribution as calculated is probably reliable. The point is that this charge distribution in the *isolated molecule* should be used with care to interpret chemical reactivity, because the latter depends on the properties of the molecule *in the transition state* and, although in some cases induced polarisability runs parallel to the permanent one (as seems to be largely the case in pyrazolopyrimidines), this is not generally so.[7] This is illustrated in the Table of localisation energies [8] for nucleophilic, electrophilic, and radical attacks on $C_{(2)}$, $C_{(6)}$, and $C_{(8)}$ of purine (I), pyrazolo-(5′ : 4′-4 : 5)pyrimidine (II), and pyrazolo(4′ : 5′-4 : 5)pyrimidine (III). These energies measure approximately the relative activation energies for such attacks and, consequently, the smaller these energies the greater should be the reactivity of the corresponding carbon atoms.

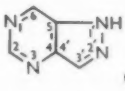
The results show that $C_{(6)}$ of purine should be more reactive towards nucleophilic attack than $C_{(2)}$ in spite of its being less positive in the isolated molecule. We have also calculated the localisation energies for nucleophilic attack on $C_{(2)}$ and $C_{(6)}$ of 2 : 6-diaminopurine as 2·730β and 2·608β respectively, again confirming the greater reactivity of $C_{(6)}$ of disubstituted purines. A striking example of a possible divergence between charge distribution

Compound	Carbon atom	Localisation energy (in β units) for Nucleophilic attack	Electrophilic attack	Radical attack	π-Electronic charge in the isolated molecule (e)
(I)	2	2·323	2·567	2·445	0·902
	6	2·176	2·482	2·329	0·907
	8	2·176	2·393	2·285	0·895
(II)	2	2·277	2·613	2·445	0·890
	6	2·115	2·529	2·322	0·881
	3′	2·535	2·213	2·374	1·053
(III)	2	2·359	2·609	2·484	0·910
	6	2·193	2·549	2·371	0·910
	3′	2·601	2·189	2·395	1·075

The values of the coulombic and exchange integrals adopted for the hetero-atoms are, in the usual notations, $\alpha_N = \alpha_C + 0{\cdot}4\beta_{C-C}$, $\alpha_{N-H} = \alpha_C + \beta_{C-C}$, $\beta_{C-N} = \beta_{C-C}$, $\beta_{C-NH} = 0{\cdot}9\beta_{C-C}$. The absolute values of the polarisation energies depend of course on the precise values of these parameters. Nevertheless, the relative values of these energies, which alone interest us here, are to a very large extent independent of the precise values of the parameters.


(I)


(II)


(III)

and reactivity is seen in electrophilic reactions of purine: the smallest localisation energy for electrophilic attack is that of $C_{(8)}$, which should thus be the most reactive towards such an attack, although it has in the ground state of isolated purine the greatest deficiency in π-electrons. The theoretical results relating to the electrophilic localisation energy agree well with Albert's findings.[9]

[6] Lynch, Robins, and Cheng, *J.*, 1958, 2973.
[7] See, *e.g.*, Pullman, *Cahiers Phys.*, 1954, **48**, 42.
[8] Wheland, *J. Amer. Chem. Soc.*, 1942, **64**, 900; Pullman and Pullman, " Les Théories Electroniques de la Chimie Organique," Masson, Paris, 1952, Chap. X; " Cancérisation par les Substances Chimiques et Structure Moléculaire," Masson, Paris, 1955, Chap. II.
[9] Albert, in " The Chemistry and Biology of Purines," Ciba Foundation Symposium, Churchill, London, 1957, p. 97.

A similar situation holds for the basicity of the ring nitrogen atoms which does not depend necessarily on the electrical charge of these atoms but must be calculated in a suitable way.[10] Thus, the most basic nitrogen should be $N_{(1)}$ in purine and adenine and $N_{(7)}$ in guanine,[4] although these are not the most charged nitrogen atoms in these molecules. Under the assumption that reactivity is correlated with the stability of the Wheland-type transition state,[8] these predictions are verified by recent experimental results such as the formation of adenine N^1-oxide[11] or the preferential reactivity of $N_{(7)}$ of guanine[12] and $N_{(1)}$ of adenine[13] towards alkylating agents. In connection with Lynch, Robins, and Cheng's speculation[6] we add that our calculations[5] indicate that $N_{(1)}$ is the most basic nitrogen atom in the active antagonist 6-aminopyrazolo(5′ : 4′-4 : 5)pyrimidine as well as in a number of other compounds of this group. Contrariwise, in the inactive antagonist, 6-aminopyrazolo(4′ : 5′-4 : 5)pyrimidine, and in other compounds of this group, the most basic nitrogen should be, following our calculations, $N_{(3)}$. The significance of these results for the possible correlation between structure and antitumour activity of both purines and pyrazolopyrimidines is discussed in references 4 and 5.

We thank the Public Health Service (U.S.A.) for a grant.

LABORATOIRE DE CHIMIE THEORIQUE, 34 RUE D'ULM, PARIS V^e^. [*Received, November 14th*, 1958.]

[10] Nakajima and Pullman, *J. Chim. phys.*, 1958, 793.
[11] Stevens and Brown, *J. Amer. Chem. Soc.*, 1958, **80**, 2759.
[12] Lawley, *Proc. Chem. Soc.*, 1957, 290; Lawley and Wallik, *Chem. and Ind.*, 1957, 633.
[13] Lawley, personal communication.

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316. *Spectral Shift in Methylpyridines.*

By ASISH KUMAR CHANDRA and SADHAN BASU.

INTRODUCTION of a methyl group into an aromatic hydrocarbon shifts the longest-wavelength absorption band. For alternant hydrocarbons the shift is bathochromic, but for non-alternant ones it may be bathochromic or hypsochromic. If it is assumed that the longest-wavelength absorption band is associated with the energy change in the transition of an electron from the highest bonding to the lowest antibonding orbital, this suggests that the methyl group changes the energy of one or both orbitals. Longuet-Higgins and Sowden[1] have worked out a simple perturbation method for calculating this change in orbital energies of aromatic hydrocarbons due to inductive and hyperconjugative effects of a methyl group or groups. It has been shown that with methylpyridines the shift is bathochromic except for 4-methylpyridine, where it is hypsochromic.[3] To find out how far Longuet-Higgins and Sowden's method enables us to estimate these shifts the present work was done. The theoretical basis of the method has been discussed in detail by Longuet-Higgins and Sowden.[1] The principles are as follows:

Inductive effect. When a ring hydrogen atom is replaced by a methyl group, the Coulomb integral of the methylated carbon atom is altered owing to the inductive effect of the electron-releasing methyl group. If a and b refer to the highest filled and the lowest empty molecular orbital respectively, the net change in transition energy due to the inductive effect is given by

$$(\Delta\varepsilon_{ab})_{\text{induc.}} = (\varepsilon_b' - \varepsilon_a') - (\varepsilon_b - \varepsilon_a) = (c_{br}^2 - c_{ar}^2)\delta\alpha_r + \left(\sum_{j\neq b}\frac{c_{br}^2 c_{jr}^2}{\varepsilon_b - \varepsilon_j} - \sum_{j\neq a}\frac{c_{ar}^2 c_{jr}^2}{\varepsilon_a - \varepsilon_j}\right)$$

where the primed quantities refer to methylpyridine carrying the methyl group at the rth carbon atom, and the unprimed to pyridine itself. c_{rj} refers to atomic-orbital coefficient of the rth carbon in the jth molecular orbital. $\delta\alpha_r$, the alteration in the Coulomb integral, was taken as $-0{\cdot}1\beta$. The molecular-orbital calculation on pyridine was made by the straightforward method, the Coulomb integral for nitrogen being taken as $(E_0 + 0{\cdot}66\beta)$

[1] Longuet-Higgins and Sowden, *J.*, 1952, 1404; cf. Coulson, *Proc. Phys. Soc.*, 1952, *A*, **65**, 933.

(E_0 being the Coulomb integral for aromatic carbon), and for carbon attached to nitrogen as ($E_0 + 0{\cdot}083\beta$) and all resonance integrals being set equal to $\beta = \beta_{C-C}$. The effect of two or more methyl groups was considered as additive. $(\Delta\varepsilon_{ab})_{\text{induc.}}$ calculated for various mono-, di-, and tri-methylpyridines are summarised in Table 1.

Hyperconjugative effect. If pyridine and methyl group are considered as two separate conjugated systems, then it can be shown by Coulson–Longuet-Higgins perturbation treatment [2] that the orbital energies of the two systems will change if they are joined by a single bond across which conjugation can be established between the two systems. If β_{rs} is the resonance integral of the bond formed between the rth carbon atom of pyridine and the sth carbon atom of the methyl group, then Longuet-Higgins and Sowden [1] showed that the energy change due to hyperconjugative effect can be written as

$$(\Delta\varepsilon_{ab})_{\text{hypercon.}} = \beta_{rs}^2 \left(\sum_{k \neq b} \frac{c_{br}^2 c_{ks}^2}{\varepsilon_b - \varepsilon_k} - \sum_{k \neq a} \frac{c_{ar}^2 c_{ks}^2}{\varepsilon_a - \varepsilon_k} \right)$$

A conjugating methyl group was considered as $-C{\equiv}H_3$ with the following Coulomb and resonance parameters: $E_c = E_0 - 0{\cdot}1\beta$, $\beta_{Me} = 2{\cdot}5\beta$, $E_{H_s} = E_0 - 0{\cdot}5\beta$, and $\beta_{rs} = 0{\cdot}7\beta$. As for the inductive effect, the hyperconjugative effect of more than one methyl group was also considered as additive. Calculated values of $(\Delta\varepsilon_{ab})_{\text{hypercon.}}$ are in Table 1. The mere addition of the two separate effects to get the resultant effect is justified in this approximation, so $(\Delta\varepsilon_{ab})_{\text{total}} = (\Delta\varepsilon_{ab})_{\text{induc.}} + (\Delta\varepsilon_{ab})_{\text{hypercon.}}$. $\Delta\lambda$ is the energy difference converted into wavelength (mμ) calculated by taking $\beta = -23{,}000$ cm.$^{-1}$, and the found values are those of Andon, Cox, and Herington.[3]

TABLE 1. *Calculated and experimental spectral shift in methylpyridines* ($\varepsilon_b - \varepsilon_a = -1{\cdot}811\beta$).

Pyridine	$(\Delta\varepsilon_{ab})_{\text{induc.}}$	$(\Delta\varepsilon_{ab})_{\text{hypercon.}}$	$(\Delta\varepsilon_{ab})_{\text{total}}$	$\Delta\lambda$ (calc.) (mμ)	$\Delta\lambda$ (obs.) (mμ)
2-Methyl	$+0{\cdot}0123\beta$	$+0{\cdot}0467\beta$	$+0{\cdot}0590\beta$	8·0	7·0
3- ,, ...	$+0{\cdot}0183\beta$	$+0{\cdot}0409\beta$	$+0{\cdot}0592\beta$	8·1	6·5
4- ,, ...	$-0{\cdot}0308\beta$	$+0{\cdot}0067\beta$	$-0{\cdot}0241\beta$	−3·2	−3·0
2 : 3-Dimethyl	$+0{\cdot}0306\beta$	$+0{\cdot}0876\beta$	$+0{\cdot}1182\beta$	16·8	11·0
2 : 4- ,, ...	$-0{\cdot}0185\beta$	$+0{\cdot}0534\beta$	$+0{\cdot}0349\beta$	4·7	3·0
3 : 4- ,, ...	$-0{\cdot}0125\beta$	$+0{\cdot}0476\beta$	$+0{\cdot}0351\beta$	4·7	2·0
2 : 5- ,, ...	$+0{\cdot}0306\beta$	$+0{\cdot}0876\beta$	$+0{\cdot}1182\beta$	16·8	14·0
2 : 6- ,, ...	$+0{\cdot}0246\beta$	$+0{\cdot}0934\beta$	$+0{\cdot}1181\beta$	16·7	14·0
3 : 5- ,, ...	$+0{\cdot}0366\beta$	$+0{\cdot}0818\beta$	$+0{\cdot}1184\beta$	16·8	12·0
2 : 3 : 6-Trimethyl ...	$+0{\cdot}0429\beta$	$+0{\cdot}1343\beta$	$+0{\cdot}1773\beta$	26·0	19·0
2 : 4 : 6- ,, ...	$-0{\cdot}0062\beta$	$+0{\cdot}1001\beta$	$+0{\cdot}0939\beta$	13·1	10·0
2 : 3 : 4- ,, ...	$-0{\cdot}0002\beta$	$+0{\cdot}0943\beta$	$+0{\cdot}0941\beta$	13·2	10·5
2 : 4 : 5- ,, ...	$-0{\cdot}0002\beta$	$+0{\cdot}0943\beta$	$+0{\cdot}0941\beta$	13·2	10·5
2 : 3 : 5- ,, ...	$+0{\cdot}0489\beta$	$+0{\cdot}1286\beta$	$+0{\cdot}1774\beta$	26·0	20·0

Agreement between the calculated and experimental shift is fairly good. The calculation shows that the spectral shift is bathochromic for all except 4-methylpyridine, as is actually the case. Whenever the methyl group is at the 4-position the inductive effect opposes the hyperconjugative effect, but the latter outweighs the former except in 4-methylpyridine.

The experimental values (Table 1) refer to methylpyridines in 0·1M-hydrochloric acid, *i.e.*, to the protonated forms. The agreement between the calculated and experimental shift is equally good for neutral forms, *i.e.*, the spectra of methylpyridines in 0·1M-sodium hydroxide. This suggests that it would be interesting to analyse the rôle of the Coulomb integral of the nitrogen atom in determining the magnitude and direction of the calculated spectral shift.* We therefore repeated the calculation for 2- and 4-methylpyridines, taking the Coulomb integral for nitrogen as $E_0 + 1{\cdot}0\beta$ and $E_0 + 0{\cdot}2\beta$ respectively; the results are summarised in Table 2.

* We thank a Referee for making this suggestion.

[2] Coulson and Longuet-Higgins, *Proc. Roy. Soc.*, 1947, *A*, **191**, 39.
[3] Andon, Cox, and Herington, *Trans. Faraday Soc.*, 1954, **50**, 918.

TABLE 2. *Rôle of Coulomb integral of nitrogen on the spectral shift of methylpyridines.*

Pyridine	Coulomb integral of N	$(\Delta\varepsilon_{ab})_{induc.}$	$(\Delta\varepsilon_{ab})_{hypercon.}$	$(\Delta\varepsilon_{ab})_{total}$
2-Methyl	$E_0 + 1{\cdot}00\beta$	$+0{\cdot}00999\beta$	$+0{\cdot}04854\beta$	$+0{\cdot}05858\beta$
	$E_0 + 0{\cdot}66\beta$	$+0{\cdot}01230\beta$	$+0{\cdot}04670\beta$	$+0{\cdot}05900\beta$
	$E_0 + 0{\cdot}20\beta$	$+0{\cdot}02800\beta$	$+0{\cdot}04540\beta$	$+0{\cdot}07340\beta$
4-Methyl	$E_0 + 1{\cdot}00\beta$	$-0{\cdot}03004\beta$	$+0{\cdot}00383\beta$	$-0{\cdot}02621\beta$
	$E_0 + 0{\cdot}66\beta$	$-0{\cdot}03080\beta$	$+0{\cdot}00670\beta$	$-0{\cdot}02410\beta$
	$E_0 + 0{\cdot}20\beta$	$-0{\cdot}03266\beta$	$+0{\cdot}01241\beta$	$-0{\cdot}02025\beta$

As the Coulomb integral is reduced the magnitude of the inductive and the hyperconjugative effect increases. In 4-methylpyridine the inductive effect is negative in all three cases, and its magnitude increases as the Coulomb integral is reduced, while the total effect becomes less negative. The lowering of the magnitude of total effect is understood as we expect the shift to become bathochromic when the Coulomb integral of nitrogen is set equal to E_0, *i.e.*, when we go over to benzene.* In these circumstances we also expect the inductive effect to become positive, but the reverse is the case. It is also evident from Table 2 that for 2-methylpyridine the bathochromic shift increases as the Coulomb integral on nitrogen is reduced. All these facts indicate that the calculated shift is dependent on the value of the Coulomb integral of nitrogen.

Atomic-orbital coefficients of pyridine are appended at a Referee's request. The y direction is $1 \longrightarrow 4$ in the pyridine nucleus, and values are based on E_N (Coulomb integral of N) $= E_0 + 0{\cdot}6600\beta$ and E_C (Coulomb integral of C attached to N) $= E_0 + 0{\cdot}0825\beta$.

Energy levels	Symmetry	$C_{(1)}$	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$
$E_0 + 2{\cdot}1837$	S_y	0·56027	0·42687	0·33667	0·30831
$E_0 + 1{\cdot}2225$	S_y	0·54867	0·15291	−0·37435	−0·61055
$E_0 + 1{\cdot}0420$	A_y	0	0·50723	0·48685	0
$E_0 - 0{\cdot}7694$	S_y	0·54540	−0·39161	−0·21180	0·55460
$E_0 - 0{\cdot}9598$	A_y	0	0·49511	−0·51570	0
$E_0 - 1{\cdot}8941$	S_y	0·29570	−0·37760	0·45061	−0·47590

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317. *Force Constants and Centrifugal Distortion in* OCS, ClCN, *and* BrCN.

By W. J. JONES, W. J. ORVILLE-THOMAS, and U. OPIK.

THE potential function is the most important single functional representation of the ground state of a molecule. The calculation of force constants is of great value in the study of molecular structure and especially of hybrid linkages, but it has been difficult to obtain precise values where sufficient isotopic frequencies are unavailable.

An unsymmetrical linear triatomic molecule of bond-lengths r_1 and r_2 and atomic masses m_1, m_2, and m_3, has two parallel stretching vibrations and the potential function governing them contains three force constants—two bond-stretching force constants, f_{11} and f_{22}, and a bond–bond interaction constant, f_{12}. Hence an infinite number of possible sets of the three force constants will reproduce the two experimental vibrational frequencies. A general method of obtaining these allowed solutions for the force constants in terms of a parameter p has been described;[1] the variation of the force constants with p for OCS is shown in the Figure. This method was applied in several cases[1,2] and a reasonable set of

* Presented at the European Spectroscopic Conference, Freiburg i. Br., Germany, July, 1957.

[1] Orville-Thomas, *J. Chem. Phys.*, 1951, **19**, 1162.
[2] Orville-Thomas, *J.*, 1952, 2383; *Trans. Faraday Soc.*, 1953, **49**, 855.

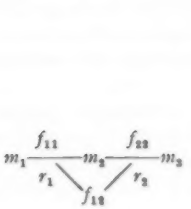
force constants chosen for each molecule by use of Gordy's relations connecting bond-order, bond-length, and force constant.[3]

Recently a new approach has become possible. Molecules are not strictly rigid and as one rotates the valence bonds and angles are distorted by centrifugal force. The extent of the distortion depends inversely upon the force constants, so knowledge of centrifugal distortion constants should yield information concerning the force field governing the vibrations of molecules.

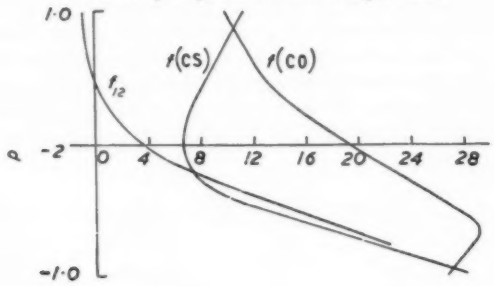
Mathematical Formulation.—When centrifugal distortion is taken into account, the frequencies of the lines in the rotational spectrum for a linear molecule are given by

$$\nu = 2B(J+1) - 4D(J+1)^3 \qquad [J \longrightarrow J+1]$$

where B is related to the moment of inertia of the molecule and J is the rotational quantum number for the lower state. The centrifugal distortion constant, D, is very much smaller



Variation of the force constants with p in OCS.



than the rotational constant B and accurate measurements of it have only been possible by microwave techniques.

Since centrifugal distortion only adds a small correction term to the rotational energy, a small error in the measuring of the frequencies of the microwave rotational absorption bands leads to a large error in the determination of D. As a molecule rotates faster the bonds tend to be distorted to a greater extent than for low J transitions. This increases the importance of the distortion correction term, which depends upon $(J+1)^3$, and so accurate values for centrifugal distortion constants can be obtained by the study of higher J transitions. Many accurate values for centrifugal distortion constants have come from measurements at millimetre and submillimetre wavelengths at Duke University.

For diatomic molecules D and f are related by $D = 16\pi^2 B^3 \mu / f$, where μ is the reduced mass of the molecule. This expression gives force constants directly from centrifugal distortion constants from rotational spectra.

For linear triatomic molecules the position is more complicated since D depends upon three force constants as well as the moment of inertia.

Using first-order perturbation theory, Kivelson and Bright Wilson [4] obtained a general expression for the energy of a non-rigid asymmetric rotor. In their theory the effect of centrifugal distortion on the energy levels is treated as an addition perturbation in which the distortion constants enter linearly. They introduce general distortion constants $\tau_{\alpha\beta\gamma\delta}$ which are related to the moments of inertia of the molecule and the force constants occurring in the most general quadratic potential function by the equation:

$$\tau_{\alpha\beta\gamma\delta} = -\tfrac{1}{2} \sum_{i,j} \frac{1}{I_{\alpha\alpha} I_{\beta\beta} I_{\gamma\gamma} I_{\delta\delta}} \left[\frac{\partial I_{\alpha\beta}}{\partial r_i}\right] \left[\frac{\partial I_{\gamma\delta}}{\partial r_j}\right] [f^{-1}]_{ij}$$

[3] Gordy, *J. Chem. Phys.*, 1947, **15**, 305.
[4] Kivelson and Bright Wilson, jun., *J. Chem. Phys.*, 1953, **21**, 1236; 1954, **22**, 904.

where terms are as defined in ref. 4. For an unsymmetrical triatomic molecule $D = -\tau h^4/64\pi^4$ and since the system has only one moment of inertia, I, we have:

$$D = \frac{h^4}{128\pi^4 I^4}\left[\left(\frac{\partial I}{\partial r_1}\right)^2 (f^{-1})_{11} + \left(\frac{\partial I}{\partial r_2}\right)^2 (f^{-1})_{22} + 2\left(\frac{\partial I}{\partial r_1}\right)\left(\frac{\partial I}{\partial r_2}\right)(f^{-1})_{12}\right] \quad . \quad . \quad (1)$$

where $\dfrac{\partial I}{\partial r_1} = 2m_1\left[\dfrac{(m_2+m_3)r_1 + m_3 r_2}{m_1+m_2+m_3}\right]$; $\dfrac{\partial I}{\partial r_2} = 2m_3\left[\dfrac{(m_1+m_2)r_2 + m_1 r_1}{m_1+m_2+m_3}\right]$

$$(f^{-1})_{11} = \frac{f_{22}}{f_{11}f_{22} - f_{12}^2};\ (f^{-1})_{22} = \frac{f_{11}}{f_{11}f_{22} - f_{12}^2};\ (f^{-1})_{12} = \frac{-f_{12}}{f_{11}f_{22} - f_{12}^2}$$

By substitution of the various possible sets of force constants in eqn. (1) values for D can be calculated and compared with the experimental value. Thus for a particular molecule it is possible to choose a set of force constants compatible with the infrared vibrational spectrum and which also yields distortion frequency shifts in accord with those obtained from direct analysis of the rotational spectrum.

Since the calculated value of the centrifugal distortion constant is critically dependent upon the values taken for the force constants, an accurate determination of the " best " set of force constants depends upon accurate determination of the former. Where this exists the overall accuracy in the determination of force constants is superior to that hitherto attained by the use of isotopic frequencies alone.

However, no account has been taken of the anharmonicity of the potential function. Another factor tending to limit the accuracy of the force-constant determination is the use of non-equilibrium bond lengths in the calculation.

Experimental.—Frequencies assigned to the stretching modes of some linear triatomic molecules are given in Table 1, together with bond-lengths obtained by microwave methods. From the frequencies in Table 1 various possible sets of force constants were obtained and the value of D corresponding to each set was calculated through eqn. (1). The calculated value for D is quite sensitive to the values chosen for the force constants. By comparison of the calculated D values with experimental ones the best set of force constants was chosen for each molecule (Table 2).

TABLE 1. *Bond-stretching frequencies* ($cm.^{-1}$) *and bond lengths* (Å) *of linear triatomic molecules.*

	ν	ν	r_1	r_2	Ref.
ClCN	2201	729	1·630	1·163	*a*, *b*
BrCN	2187	580	1·789	1·160	*a*, *b*
OCS	2064	859	1·161	1·560	*b*, *c*

[a] Herzberg, " Molecular Spectra and Molecular Structure," Van Nostrand, New York, 1945, Vol. 2, p. 174. [b] Smith, Ring, Smith, and Gordy, *Phys. Rev.*, 1948, **74**, 123, 370; Townes, Merrit, and Wright, *ibid.*, p. 1113. [c] Callomon, McKean, and Thompson, *Proc. Roy. Soc.*, 1951, *A*, **208**, 341.

TABLE 2. *Force constants for* ClCN, BrCN, *and* OCS.

f (10^5 dynes/cm.)				D (10^{-3} Mc./sec.)	
f_{11}	f_{22}	f_{12}		Calc.	Exptal.[a]
4·76 ± 0·02	18·45 ± 0·10	1·33 ± 0·01	^{35}ClCN, ^{37}ClCN	1·662, 1·600	$1{\cdot}66_3$, $1{\cdot}60_6$
4·00 ± 0·02	17·76 ± 0·10	0·70 ± 0·01	^{79}BrCN, ^{81}BrCN	0·8844, 0·875	$0{\cdot}884_4$, $0{\cdot}871_6$
15·35 ± 0·10	7·32 ± 0·04	0·96 ± 0·01	OC^{32}S	1·310	$1{\cdot}31_0$

[a] Burrus and Gordy, *Phys. Rev.*, 1956, **101**, 599.

EDWARD DAVIES CHEMICAL LABORATORIES AND DEPARTMENT OF APPLIED MATHEMATICS, UNIVERSITY COLLEGE OF WALES, ABERYSTWYTH. [*Received, November 24th*, 1958.]

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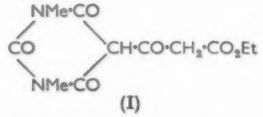
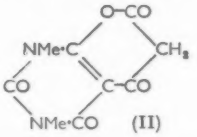
318. *Preparation of* 1 : 3-*Dimethylbarbituric Acid and Formation of* 5-*Ethoxycarbonylacetyl*-1 : 3-*dimethylbarbituric Acid.*

By J. W. Clark-Lewis and M. J. Thompson.

Barbituric acids are usually prepared from mono- or di-substituted malonic esters and urea or substituted ureas by condensation with the aid of a sodium alkoxide, but this procedure appears less satisfactory for those acids not carrying 5-substituents, which are obtained in better yield from malonic acid and ureas with acetic anhydride as condensing agent.[1] 1 : 3-Dimethylbarbituric acid was required in larger quantities than had previously been prepared, and repetition of the synthesis according to Biltz and Wittek [1] but with sixfold quantities gave material heavily contaminated with a by-product, m. p. 112°; formation of the latter was suppressed, and a satisfactory yield of 1 : 3-dimethylbarbituric acid obtained, by adding the acetic anhydride more slowly. The structure (I) proposed for



(I)



(II)

the by-product rests on elementary analysis and the titration equivalent with sodium hydroxide, which gave the empirical formula $C_{11}H_{14}O_6N_2$, and the development with ferric chloride of a red colour, indicative of the β-keto-ester structure. The main features of this structure are confirmed by formation of the compound from 1 : 3-dimethylbarbituric acid, malonic acid, and acetic anhydride; this condensation we suppose to give initially the enol lactone ester (II) which, during crystallisation from ethanol, is converted into the ethyl ester (I). The ethoxycarbonylacetyl compound (I) was hydrolysed slowly by hot concentrated hydrochloric acid to 1 : 3-dimethylbarbituric acid.

Experimental.—1 : 3-*Dimethylbarbituric acid.* Acetic anhydride (120 c.c.) was added dropwise during 3 hr. to a stirred solution of *sym.*-dimethylurea (32 g.) and malonic acid (36 g.) in acetic acid (80 c.c.). During the addition, and thereafter for 30 min., the temperature was kept at 65—70°, and the temperature was then raised and kept at 90° for 4 hr. The solution was evaporated under reduced pressure, and the residue was boiled for 15 min. with ethanol (200 c.c.); 1 : 3-dimethylbarbituric acid (33·5 g., 60%) crystallised from the cold ethanolic solution in long flat needles, m. p. 121—122° raised by recrystallisation from ethanol or benzene to 122—123° (lit.,[1] 123° and [2] 122—123°). Refrigeration of the mother liquors gave a crystalline mixture (8 g.) which yielded more (4·6 g.) dimethylbarbituric acid (total 38·1 g., 68%) after recrystallisation from benzene. Concentration of the filtrate, addition of hexane, and crystallisation of the resulting solid from ethanol gave 5-*ethoxycarbonylacetyl*-1 : 3-*dimethylbarbituric acid* in needles (2·55 g.), m. p. 110—111°, raised by recrystallisation to m. p. 112° (Found: C, 48·9; H, 5·3; N, 10·0; OEt, 14·4%; equiv., 270. $C_{11}H_{14}O_6N_2$ requires C, 48·9; H, 5·2; N, 10·4; OEt, 16·7%; equiv., 270·2). A larger yield of the by-product was obtained when the acetic anhydride was added more quickly (30 min.).

5-*Ethoxycarbonylacetyl*-1 : 3-*dimethylbarbituric acid* (I). 1 : 3-Dimethylbarbituric acid (7·8 g.), malonic acid (7 g.), acetic acid (20 c.c.), and acetic anhydride (7 c.c.) were heated at 70° for 13 hr., before evaporation under reduced pressure. The residue was boiled with ethanol (50 c.c.) for 1 hr., and 1 : 3-dimethylbarbituric acid (2·6 g.), m. p. 121—122°, crystallised from the cold solution. Refrigeration caused crystallisation of more material (3·9 g.), m. p. 70—85°, which was separated by crystallisation from benzene into 1 : 3-dimethylbarbituric acid (1·2 g.; total recovery 3·8 g., 49%), m. p. 120—122°, and 5-ethoxycarbonylacetyl-1 : 3-dimethylbarbituric acid (2·1 g.), m. p. 110—111°, after crystallisation from ethanol. The ethoxycarbonyl compound was identical with the by-product, m. p. 112°, obtained in the preparation

[1] Biltz and Wittek, *Ber.*, 1921, **54**, 1035.
[2] Cope, Heyl, Peck, Eide, and Arroyo, *J. Amer. Chem. Soc.*, 1941, **63**, 356.

of dimethylbarbituric acid, and was very soluble in benzene, sparingly soluble in cold ethanol, and insoluble in light petroleum; an alcoholic solution of the β-keto-ester gave a red colour with ferric chloride.

Hydrolysis of 5-ethoxycarbonylacetyl-1 : 3-dimethylbarbituric acid. The ester (1 g.) was heated on a steam-bath with concentrated hydrochloric acid (20 c.c.) for 14 hr. before evaporation of the solution to dryness under reduced pressure. Crystallisation of the residue from ethanol gave 1 : 3-dimethylbarbituric acid (0·35 g., 60%), m. p. 120—122° raised by recrystallisation to m. p. and mixed m. p. 122—123°.

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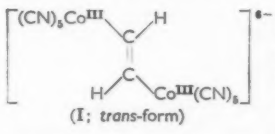
319. *An Acetylene-cyanide Complex of Cobalt*(III).

By W. P. GRIFFITH and G. WILKINSON.

DURING recent studies [1] on the pentacyanocobaltate(II) ion, it has been found that its aqueous solutions absorb various gases; we, and Winfield,[2] have observed the uptake of acetylene to give yellow solutions. From these solutions we have isolated a yellow crystalline potassium salt of stoicheiometry $K_6[Co_2(CN)_{10}C_2H_2],4H_2O$. This is diamagnetic, readily soluble in water, and thermally somewhat unstable, decomposing *in vacuo* at ~70°; it is also slowly decomposed by air. The salt was also prepared in deuterium oxide solution as $K_6[Co_2(CN)_{10}C_2H_2],4D_2O$.

It appears unlikely that in this complex ion the acetylene portion is bound to the metal atoms by donation of π-electrons from the multiple bonds to the metal atoms as in the cobalt carbonyl–acetylene complexes [3] such as $Co_2(CO)_6C_2H_2$, since such a formulation, as well as requiring a metal–metal bond, would lead to the inert-gas structure for the metal atom being exceeded.



(I; *trans*-form)

We suggest that a more reasonable structure for the complex ion is of the type (I), where a tervalent cobalt atom in an octahedral or somewhat distorted octahedral situation is bound to five cyanide groups and to an ethylene group. Such a formulation would give a diamagnetic ion with each cobalt atom having an inert-gas configuration. It may be noted that structure (I) resembles the structure recently suggested [4] for the black nitrosopentamminocobalt cation where a hyponitrito-group bridges the two cobalt atoms.

Spectroscopic studies generally support the formulation (I). Thus the high-resolution nuclear magnetic resonance spectrum (in D_2O solution) of the ion shows a single proton resonance line in the olefinic region, at 64 cycles/sec. (at 40 Mc./sec.) on the low-field side relative to water at 21° ± 1° c.

The infrared spectra of both the hydrate and the deuterate were measured. In addition to the expected absorption bands for H_2O and D_2O, there are in both compounds sharp absorption bands at 2980m, 2140vs, 2115vs, 1615m, 1120m, and 975m cm.$^{-1}$. The band at 2980 cm.$^{-1}$ is clearly assignable as a C–H stretching frequency; this value is consideraby lower than those for acetylenes, and indeed is somewhat lower than the usual frequency range for olefinic C–H stretching modes.[5] The two very strong bands at 2140 and 2115 cm.$^{-1}$ are unquestionably stretching bands for the cyanide groups. The band at 1615 cm.$^{-1}$ may be reasonably ascribed to a C=C vibration [5] and the value again indicates

[1] Winfield, *J. Amer. Chem. Soc.*, 1958, **80**, 2060; Griffith and Wilkinson, *J. Inorg. Nuclear Chem.*, 1958, **7**, 295; Griffith, Pratt, and Wilkinson, *Nature*, 1958, **182**, 466.
[2] Winfield, personal communication.
[3] Greenfield, Sternberg, Friedel, Wotiz, Markby, and Wender, *J. Amer. Chem. Soc.*, 1956, **78**, 120.
[4] Griffith, Lewis, and Wilkinson, *J. Inorg. Nuclear Chem.*, 1958, **7**, 38.
[5] Bellamy, "The Infra-red Spectra of Complex Molecules," 2nd edn., Methuen and Co., London, 1958, p. 43.

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that the triple-bond character of the acetylene has been reduced in the ion to that of a double bond; the shift to lower wave numbers is greater in our ion than in the stable acetyleneplatinum complexes [6] where, however, there was only one acetylene residue per metal atom in a mononuclear complex so that the situations are of course not comparable. Although such C=C vibrations are reported to be symmetry-forbidden in the infrared region for *trans*-alkenes,[7] they do appear at low intensities in some *trans*-compounds.[8] The appearance of a fairly strong band for our ion might on this basis only imply a non-*trans*-form. The band at 1120 cm.$^{-1}$ may be attributed to an in-plane C–H deformation; although this should again be inactive in the infrared region, strong absorptions have been observed in alkenes in the 1200—1400 cm.$^{-1}$ region.[9] Finally, the band at 975 cm.$^{-1}$ may be assigned to a C–H bending mode with the hydrogen atom out of the plane of the double bond; these vibrations are known [10] to fall in the range 990—965 cm.$^{-1}$ and also to occur only for non-*cis*-types of system.[11]

Thus while we cannot be specific concerning the question of *cis*- or *trans*-structures on the basis of infrared spectra, particularly since the spectra had to be obtained in solid-state mulls, and since no other established complex of a similar type with transition metals and of known structure is available for comparison, we believe that the *trans*-form is more likely. The appearance of both the 975 cm.$^{-1}$ and the 1615 cm.$^{-1}$ band suggests that there is probably some distortion from a strictly *trans*-configuration and deviations from non-planarity about the double bond are likely. A *cis*-form, even if distorted, seems sterically unlikely in view of the presence of the approximately octahedrally disposed cyanide groups around the metal atoms.

Experimental.—Acetylene gas was passed into an air-free solution of hydrated cobaltous chloride (2·38 g., 0·01M) and potassium cyanide (3·25 g., 0·05M) with external ice-cooling. The deuterate was made similarly from anhydrous cobaltous chloride under anhydrous conditions. After a few minutes, the solution changed from deep green to straw yellow. The addition of air-free ethanol precipitated a yellow-brown oil which quickly crystallised; the crystals of *hexapotassium decacyanoacetylenedicobaltate tetrahydrate* were dissolved in water, re-precipitated from ethanol, washed with ethanol and ether, and dried under vacuum at room temperature (yield 3 g., 85%) [Found: K, 33·8; Co, 16·6; C, 19·8; N, 20·0; H, 1·9. $K_6[Co_2(CN)_{10}C_2H_2],4H_2O$ requires K, 33·0; Co, 16·6; C, 20·3; N, 19·7; H, 1·7%].

A nickel complex was also obtained by passing acetylene into an aqueous solution of $K_4[Ni^{I}_2(CN)_6]$; the product was too unstable for satisfactory analysis. Its infrared spectrum and diamagnetism suggest a formulation $K_4[Ni^{II}_2(CN)_6C_2H_2]$ similar to that of the cobalt anion but with square planar (dsp^2) bivalent nickel.

Infrared measurements were made in Nujol and hexachlorobutadiene mulls on a Perkin-Elmer Model 21 instrument with NaCl and CaF_2 optics. High-resolution nuclear magnetic resonance measurements were made with the assistance of Dr. L. Pratt on a Varian Associates Model 4300 spectrometer; the samples were contained in spinning 5 mm. o.d. Pyrex sealed tubes, and the water line was used as reference.

Magnetic susceptibilities were measured on the solids by the Gouy method.

Thanks are offered to the Department of Scientific and Industrial Research for a maintenance grant (to W. P. G.).

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IMPERIAL COLLEGE, LONDON, S.W.7. [*Received, December 8th*, 1958.]

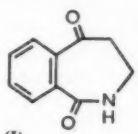
[6] Chatt, Rowe, and Williams, *Proc. Chem. Soc.*, 1957, 208.
[7] Sheppard, *J. Inst. Petroleum*, 1951, **37**, 95.
[8] Jones and Sandorfy, "Chemical Applications of Spectroscopy," Interscience Publishers Inc., New York, 1956, p. 370.
[9] Sheppard and Sutherland, *Proc. Roy. Soc.*, 1949, *A*, **196**, 195.
[10] Kilpatrick and Pitzer, *J. Res. Nat. Bur. Stand.*, 1947, **38**, 191.
[11] Rasmussen and Brattain, *J. Chem. Phys.*, 1947, **15**, 131, 135.

320. o-*Acetylbenzamide.*

By A. H. Rees.

Karslake and Huston [1] gave no details for their original preparation of *o*-acetylbenzamide from the acid by use of phosphorus pentachloride and ammonia. Winkler [2] was unable to obtain the acid chloride, using thionyl chloride, and though Halford and Weissmann [3] seem to have prepared it successfully it gave poor yields of amides.

Since the amide was a potential intermediate for the synthesis of 2 : 3 : 4 : 7-tetrahydrobenz[*e*]azepine-4 : 7-dione (I) its preparation was re-examined, and a good yield was obtained. Its reaction with formaldehyde or formic acid in attempts at forming the azaheptacycle gave only polymers. Ring formation in two stages was therefore considered and a Mannich base was prepared from *o*-acetylbenzamide. Elimination of the secondary amine was achieved but cyclisation to (I) did not occur, resins being obtained.



(I)

o-Acetylbenzamide is not stable; it slowly polymerises.

Pilot Mannich-type reactions with *m*-hydroxyacetophenone and its benzoyl ester, aimed at the preparation of azaheptacyclic ketones, were unsuccessful, but a number of new benz[*f*]azepine derivatives has been otherwise prepared and will be reported later.

Experimental.—*o*-Acetylbenzoic acid was prepared by hydrolysis of phthaloylacetic acid obtained according to Gabriel and Neumann.[4] The latter acid is best purified by refluxing it with acetic acid in which it is sparingly soluble; a sample recrystallised from dioxan had not the quoted [5] m. p. of 243—246° but 276° as given by Röser [6] (Found: C, 62·9; H, 3·30. Calc. for $C_{10}H_8O_4$: C, 63·2; H, 3·18%).

o-*Acetylbenzamide.* The acid (32·8 g.) and thionyl chloride (55 ml.) were mixed at 30° then warmed to 40°, dissolution then becoming complete. After rapid evaporation below 30° the residue, dissolved in a little dioxan, was added to aqueous ammonia (100 ml., *d* 0·88) precooled to 5°. The mixture was rapidly evaporated, and the crude amide triturated with water then filtered off and dried *in vacuo*; yield, 20·7 g. (63%), m. p. 112°. The *semicarbazone*, m. p. 216°, crystallised from alcohol (Found: N, 25·2. $C_{10}H_{12}O_2N_4$ requires N, 25·5%).

o-*Acetyl*-N-*diethylaminomethylbenzamide.* To the above amide (16·4 g.) in alcohol were added diethylamine (7·3 g.) and formaldehyde (7·5 ml., 40%). After 2 days the solution was evaporated, leaving an oil (23·7 g.) which solidified on standing. The Mannich *base* had m. p. 118° from *iso*propyl ether (Found: C, 67·2; H, 8·09; N, 11·4. $C_{14}H_{20}O_2N_2$ requires C, 67·6; H, 8·1; N, 11·3%). The *base methiodide* had m. p. 153° from alcohol (Found: C, 46·5; H, 5·9; N, 7·2; I^-, 32·4. $C_{15}H_{23}O_2N_2I$ requires C, 46·15; H, 5·94; N, 7·2; I^-, 32·5%). The *base picrate* had m. p. 126° from alcohol (Found: N, 14·8. $C_{20}H_{23}O_9N_5$ requires N, 15·2%).

Elimination of diethylamine from the Mannich base. (a) The base (0·5 g.) was heated gently and secondary amine was evolved; the cold residue was intractable. (b) The base (2·3 g.) was refluxed in toluene to which a speck of sodium had been added, and a stream of nitrogen passed through the solution to remove the secondary amine evolved; a tar was deposited. (c) The base (3·8 g.) was shaken with dilute sulphuric acid and chloroform; evaporation of the latter after washing until neutral left a resin (2·7 g.).

m-Hydroxyacetophenone was benzoylated, and the *ester* had m. p. 52° from ether, b. p. 170°/0·3 mm. (Found: C, 75·3; H, 4·9. $C_{15}H_{12}O_3$ requires C, 75·0; H, 5·06%). Its *dinitrophenylhydrazone* had m. p. 206° from acetic acid (Found: C, 60·0; H, 3·8; N, 13·1. $C_{21}H_{16}O_6N_4$ requires C, 60·0; H, 3·8; N, 13·3%); its *semicarbazone* had m. p. 222° from dioxan (Found: N, 14·2. $C_{16}H_{15}O_3N_3$ requires N, 14·2%).

The author thanks Professors F. Bergel and C. W. L. Bevan for their interest.

University College, Ibadan, Nigeria. [*Received, December 15th*, 1958.]

[1] Karslake and Huston, *J. Amer. Chem. Soc.*, 1909, **31**, 481.
[2] Winkler, *Ber.*, 1948, **81**, 256.
[3] Halford and Weissmann, *J. Org. Chem.*, 1952, **17**, 1646.
[4] Gabriel and Neumann, *Ber.*, 1893, **26**, 952.
[5] Michael and Gabriel, *Ber.*, 1877, **10**, 392.
[6] Röser, *Ber.*, 1884, **17**, 2620.

321. *The Preparation of Potassium Pentacyanonitrosylvanadate(−1).*

By W. P. Griffith, J. Lewis, and G. Wilkinson.

Very few nitric oxide complexes of vanadium have been characterised.[1] We have now prepared the compound $K_5[V^{-I}(CN)_5NO],H_2O$, which is a member of the isoelectronic series $[V^{-I}(CN)_5NO]^{5-}$, $[Mn^{I}(CN)_5NO]^{3-}$, $[Fe^{II}(CN)_5NO]^{2-}$; although the chromium compound $K_3[Cr^{I}(CN)_5NO],H_2O$ has been obtained,[2] we have been unable to isolate the corresponding chromium(0) compound which would be a member of this series.

The vanadium complex was prepared by the reaction of hydroxylamine hydrochloride with potassium vanadate in the presence of excess of cyanide and hydroxyl ions. It is diamagnetic and shows a N–O stretching frequency of 1575 cm.$^{-1}$, which is the lowest recorded for nitric oxide in an octahedral complex where the nitric oxide must be regarded as bonding as NO^+;[3] other strong bands in the spectrum are listed in the Table. The reason for this unusually low N–O frequency can be sought in the factors which may be considered to influence the extent of π-bonding between the metal atom and the ligands. These factors are the stereochemistry of the complex, the nature of the ligands, and the electronegativity of the metal atom. We have considered the effect of stereochemistry in nitric oxide–transition metal complexes previously.[3] The effect of the ligands for a given metal in a given oxidation state is normally quite small and is of the order of ~100 cm.$^{-1}$ as may be seen from the small variation in the N–O stretching frequencies in ruthenium complexes or in the substituted nitrosylcobalt carbonyls;[3] the frequencies in the latter compounds are given in the Table to illustrate this point.

In the series of pentacyanonitrosyl complex anions, the stereochemistry and ligand effects are constant but there is a large variation in the electronegativity of the metal atom, the formal charges on the latter varying from −1 in vanadium to +2 in iron. From the Table, it is notable that the C–N frequency does not show any substantial change whereas a large variation in the N–O frequency is observed. The small change in the C–N frequency suggests only a small change in the extent of π-bonding in the M–C–N systems. However, on decreasing the electronegativity of the metal Fe→V, the large decrease in the N–O frequency can be correlated with a greater tendency towards metal-to-nitrogen π-bonding owing to the greater availability of electron density. This would indicate that cyanide is a much better π-bonding ligand than the nitric oxide group, and it is noteworthy that the highest N–O stretching frequency occurs for a given metal in a given oxidation state in the cyanide complex, as in those of ruthenium.

There are insufficient data available on metal–ligand stretching frequencies to allow us to be certain about the above explanation. An alternative view is that the major

Infrared spectra of nitrosyl cyanide and carbonyl metal complexes.

Compound	Frequency (cm.$^{-1}$) N–O	C–N	Compound	Frequency (cm.$^{-1}$) N–O
$K_5[V(CN)_5NO]$	1575	2095	$NOCo(CO)_2[PPh_3]$	1754 [b]
$K_3[Mn(CN)_5NO]$	1730 [b]	2120	$NOCo(CO)[PPh_3]_2$	1754 [b]
$Na_2[Fe(CN)_5NO]$	1925 [a]	2152 [a]	$NOCo(CO)_2[Sb(C_7H_7)_3]$	1764 [b]
$NOCo(CO)_3$	1832 [b]		$NOCo(CO)_2[As(C_7H_7)_3]$ ...	1754 [b]

[a] Herington and Kynaston, *J.*, 1955, 3555. [b] Lewis, Irving, and Wilkinson, *J. Inorg. Nuclear Chem.*, 1958, **7**, 32.

change takes place in the extent of the metal-to-nitrogen σ-bonding on proceeding from the iron to the vanadium complex. The lower N–O stretching frequency in the latter would then arise from delocalisation of the electron density on to the oxygen atom of the nitric oxide group.

[1] Addison and Lewis, *Quart. Rev.*, 1955, **9**, 115.
[2] Griffith, Lewis, and Wilkinson, *J.*, 1959, 872.
[3] Lewis, Irving, and Wilkinson, *J. Inorg. Nuclear Chem.*, 1958, **7**, 32.

Experimental.—Microanalyses are by the Microanalytical Laboratory, Imperial College.

Potassium pentacyanonitrosylvanadate(−1), $K_3[V(CN)_5NO],H_2O$. Ammonium vanadate (5 g.) was dissolved in a cooled solution of potassium hydroxide (15 g. in 50 ml. of water), and treated with excess of potassium cyanide solution (15 g. in 100 ml. of water). The solution was then filtered and hydroxylamine hydrochloride (8 g.) was added, whereupon the solution became deep red. It was heated on the steam-bath with occasional stirring, until no more ammonia was evolved (for about 2 hr., sufficient extra water being added at intervals to prevent any crystallisation). The cooled and filtered solution was slowly added to alcohol, and the resulting orange oil separated, washed with alcohol, dissolved in water (7 ml.), and again precipitated with alcohol. The oil was then triturated with warm absolute alcohol and ether, whereupon it quickly crystallised. This procedure was repeated, and the bright orange crystals (which are deliquescent) were dried under reduced pressure; yield, 4 g. (30%) [Found: V, 12·29; K, 46·73. $K_3[V(CN)_5NO],H_2O$ requires V, 12·01; K, 46·14%].

Physical measurements. The magnetic susceptibility was measured on the solid compound by the Gouy method. Infrared spectra were taken in Nujol and hexachlorobutadiene mulls, a Perkin-Elmer Model 21 spectrophotometer being used.

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[*Received, December 29th*, 1958.]

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322. *A Convenient Preparation of* o-*Aminoaryl Cyanides.*

By G. R. BEDFORD and M. W. PARTRIDGE.

THE formation of *o*-aminophenyl cyanide by thermal decomposition of isatin 3-oxime [1,2] and the small-scale (0·1 g.) production of 2-amino-3-cyanonaphthalene in good yield from 5 : 6-benzisatin 3-oxime [3] have previously been reported. We now find that this reaction can be employed on a useful preparative scale both for *o*-aminophenyl cyanide and for those derivatives for which the corresponding isatins are readily accessible. Moreover, the method is applicable to the production of substituted *o*-aminoaryl cyanides having orientations not readily accessible by methods hitherto used.

Decomposition of the oximes is vigorous, and for a 50-g. quantity is complete in about 3 min. When no solvent is employed, provision must be made to trap the aminoaryl cyanide entrained in the evolved carbon dioxide. Borsche, Weussmann, and Fritzsche [1] record their failure to obtain any 2-amino-5-nitrophenyl cyanide from 5-nitroisatin 3-oxime, whereas we obtained this cyanide in satisfactory yield.

Experimental.—The substituted isatins [4] readily afforded their oximes (80—85%) on being boiled with hydroxylamine hydrochloride (1·1 mol.) in aqueous solution for 20 min.[5] It was found advantageous to recrystallise isatin 3-oxime from 50% aqueous ethanol.

2-Aminophenyl cyanide. Powdered isatin 3-oxime (50 g.) was placed in a 1-l. flask connected *via* a splash-head to a 2-l. two-necked flask bearing a reflux condenser connected to a Drechsel bottle containing ether. The reaction was started by melting the oxime near its upper surface and was allowed to proceed spontaneously. *o*-Aminophenyl cyanide in the Drechsel bottle, condensing system, and reaction vessels from six such decompositions was collected in ether. The ether solution was filtered and evaporated; the residue furnished the pure cyanide, b. p. 132—136°/11 mm., on distillation (yield, 144 g., 65%), m. p. 49—50°, undepressed on admixture with a specimen prepared from *o*-nitrophenyl cyanide. Its acetyl derivative had m. p. 134°; Pinnow and Sämann [6] record m. p. 133°.

[1] Borsche, Weussmann, and Fritzsche, *Ber.*, 1924, **57**, 1149.
[2] Bargellini and Turi, *Gazzetta*, 1954, **84**, 157.
[3] Etienne and Staehelin, *Bull. Soc. chim. France*, 1954, 743.
[4] Sandmeyer, *Helv. Chim. Acta*, 1919, **2**, 234; *Org. Synth.*, Coll. Vol. I, p. 327; Calvery, Noller, and Adams, *J. Amer. Chem. Soc.*, 1925, **47**, 3058.
[5] Hovorka and Sykora, *Chem. Listy*, 1938, **32**, 241.
[6] Pinnow and Sämann, *Ber.*, 1896, **29**, 631.

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2-Amino-5-methylphenyl cyanide (17·6 g., 49%) was obtained similarly from 5-methylisatin 3-oxime [7] (48 g.), b. p. 150—152°/15 mm., m. p. 59—60°; Ehrlich [8] records m. p. 60—61°.

2-Amino-5-chlorophenyl cyanide. 5-Chloroisatin 3-oxime [9] (5 g.) decomposed at 250° during 15 min. The *amino-cyanide* was collected in benzene, recovered, and, on crystallisation from water, afforded needles (2 g., 52%), m. p. 96—98° (Found: C, 54·8; H, 3·4; N, 18·2. $C_7H_5N_2Cl$ requires C, 55·1; H, 3·3; N, 18·4%).

2-Amino-3-cyanobenzoic acid. 7-Carboxyisatin 3-oxime [10] (5·1 g.) furnished a sublimate when decomposed in the same way as the foregoing example. Recrystallisation of the sublimate from aqueous ethanol gave the *amino-cyanide* (0·62 g., 16%) as needles, m. p. 280—282° (Found: C, 59·3; H, 4·0; N, 17·3. $C_8H_6O_2N_2$ requires C, 59·3; H, 3·7; N, 17·3%). This compound was amphoteric and gave a positive diazo-test.

2-Amino-5-nitrophenyl cyanide. 5-Nitroisatin 3-oxime [1] (5 g.) was heated in boiling nitrobenzene (20 ml.) for 45 min. and cooled. The solid which separated, on recrystallisation from aqueous acetone, furnished the amino-cyanide (2·6 g., 66%), m. p. 205—206°, undepressed on admixture with an authentic specimen.[11]

We thank Mr. J. D. Hunt for carrying out many preparations of *o*-aminophenyl cyanide by this method.

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[7] Meyer, *Ber.*, 1883, **16**, 2261.
[8] Ehrlich, *Ber.*, 1901, **34**, 3366.
[9] Schunck and Marchlewski, *Ber.*, 1895, **28**, 539.
[10] Rupe and Guggenbühl, *Helv. Chim. Acta*, 1927, **10**, 926, who describe this oxime erroneously as isatin 2-oxime.
[11] Baudet, *Rec. Trav. chim.*, 1924, **43**, 707.

NOTICE TO AUTHORS

Attention is drawn to the changes of convention in chemical nomenclature reported in *Proceedings* for January, 1959, page 4. The changes should be incorporated in all manuscripts submitted henceforth.

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